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EXPERIENCES WITH BATTLE WOUNDS OF THE HEAD

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THE SURGERY OF BATTLE CASUALTIES is largely concerned with the care of infected wounds and compound fractures. The general principles applicable to these injuries hold good for all regions of the body, but wounds of the head present special problems owing to certain anatomic and physiologic peculiarities of the structures involved in the scalp, skull, meninges and brain.

In the case of the scalp and skull, their liberal blood supply gives them increased resistance against virulent infections, especially those due to anaerobes, and massive necrosis and gangrene are extremely rare. On the other hand, their intricate lymphatic and venous connections through the osseous diploë, and from the brain and meninges make the persistence of apparently minor and latent sepsis in the scalp a menace likely to result in unsuspected and deeper infections at some later date.

The arrangement of the outer and inner tables in the bones of the cranial vault allows even a small missile to cause much more damage to the inner table than the outer, or than would be suspected from a superficial examination of the wound. In this connection, it is most important to realize the terrific kinetic energy ($\frac{1}{2}$ mv^2) of a missile of small mass (m) owing to its high velocity (v) at the moment of impact.

The protective barrier-like function of the dura mater is well known and every effort must be made to conserve it. Indeed, the whole prognosis of head wounds depends on whether or not it has been penetrated either by the missile itself or by pieces of indriven bone, or hat. Somewhat unexpectedly, and contrary to the experience of the Great War of 1914–1918, it has been found in this series of cases that pieces of metal from bombs, shells, *etc.*, are, in themselves, relatively innocuous inside the skull, due to the fact that the earth and sand of the desert have not been manured and contain comparatively few virulent organisms, and the missiles are almost red-hot when they enter. In fact, Major P. B. Ascroft, R.A.M.C., of another Neurosurgical Unit in the Middle East, relates how an officer patient severely burned his thumb and index finger trying to pull out a small piece of bomb splinter after it had penetrated his steel helmet and just stuck in his frontal bone, without causing any loss of consciousness! On the other hand, organic foreign bodies such as pieces of indriven bone, felt and sponge rubber from hats and steel helmets seem to form a nidus

for bacteria and are always a potential source of danger until removed. Failure to recognize their presence, especially after comparatively minor injuries, has occurred during the rush of casualties, and almost invariably serious and even fatal consequences have resulted, as will be shown later. Thus, the practice of always removing organic foreign bodies has been adopted. Inorganic foreign bodies alone have been left *in situ* if not readily accessible and provided the presence of abscess or other space-consuming lesion has been excluded by an examination of the cerebrospinal fluid, and by encephalography. It is as yet too early to tell whether their retention will be more conducive to posttraumatic epilepsy than the gliosis and scar which must remain, even after their removal.

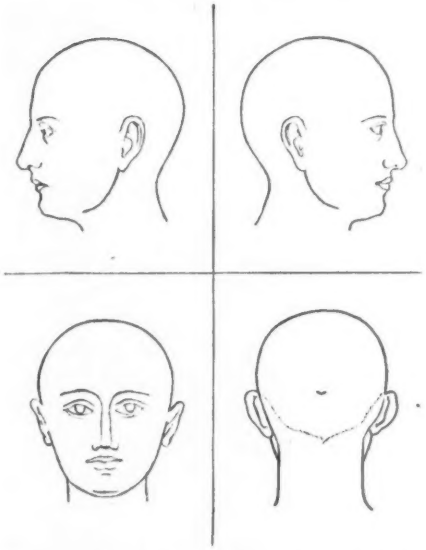
Finally, the management of wounds of the head is not a mere exercise in operative technic, even granted that adequate facilities are available. A careful neurologic examination, to determine the extent of the underlying damage to the brain (if any) must be made as early as possible, if useless and unnecessary operations are to be avoided, and if true significance is to be attached to any alteration in clinical signs which may be observed later. It must always be borne in mind that the damage done to the brain at the time of injury is irreparable, except by Nature's methods, and that operations should only be undertaken for the prevention of sepsis and the relief of compression by depressed bone, hemorrhage, or abscess. The clinical condition of the patient, varying from time to time, may be the only guide as to whether to open the dura mater or not, a most important decision to arrive at, in view of its protective function already mentioned. The method of recording these early and subsequent essential observations is shown in Figures 1 and 2 (Head Injury Card). Remember that evidence of local or focal cerebral damage, as manifested by aphasia, monoplegia, hemiplegia, visual field defects and other neurologic syndromes, is not, in itself, an indication for operation in the early stages after wounding. Such signs are common, especially after tangential nonpenetrating wounds, which may not even injure the skull. Increasing depth of unconsciousness is the cardinal sign of compression calling for urgent operative measures, and in the absence of this sign and foreign bodies (mainly bone fragments), intracranial surgical procedures should be deferred.

CLASSIFICATION AND TERMINOLOGY

A total number of 78 cases of all types were treated at this Center between July and December, 1942, during the fighting in the vicinity of El Alamein. In 25 of these cases there had been penetration of the dura mater. A review of this material indicated that open wounds of the head could be classified into the following six groups (modified from Cushing's nomenclature):

1. Scalp wounds.
2. Wounds of the skull, without depression of fragments.
3. Wounds of the skull, with depression of fragments but without penetration of the dura.

4. Wounds of the skull and brain, with penetration of the dura.
5. Perforating, or "through-and-through" wounds.
6. Penetrating or perforating wounds through the orbits, accessory nasal sinuses and mastoid air cells.



All questions marked with interrogation mark to be answered with:— + = Yes.
O = No.

MENTAL STATE.

Alert?_____ Drowsy?_____ Comatose?_____

Lucid?_____ Confused?_____

Quiet?_____ Excited?_____ Irritable?_____

PUPILS.

Dilated?_____ Pin-point?_____ Equal?_____

R. Larger?_____ L. Larger?_____

WEAKNESS OR PARALYSIS?

Right limbs?_____ Left Limbs?_____

PULSE RATE?_____ Fits?_____

RESPIRATION RATE_____

Army Form W 3118a.

HEAD INJURY CARD.

For use in Field Ambulances, Casualty Clearing Stations and all Hospitals.

At each Station or Hospital a new card must be filled in and placed with the other cards in the patient's envelope ____ A.F.W.3118A.

NAME_____ No._____
(BLOCK CAPITALS)

Rank_____ Unit_____

Date and time of injury_____

Date and time of examination_____

External injury?_____ If fracture seen?_____

Fissured?_____ Depressed?_____

(Site of external wounds to be marked on diagrams on back of this card)

152 G.H.Q. P./10,000/12-41

TREATMENT GIVEN.

Morphia given?_____ Dose_____

Sulphonamide given?_____

A.T.S. given?_____

PROGRESS UNDER OBSERVATION.

Improved?_____ Stationary?_____ Worse?_____

REMARKS:—

Signature of M.O.

FIG. 1 and 2.—Head Injury Card, showing four sides.

Wounds in Groups 3, 4, 5 and 6 should be regarded as severe.

Wounds caused by bullets from revolvers, rifles, light automatic weapons ("tommy-guns") and machine guns (all types) were called "gunshot wounds," or "G.S.W."

Wounds caused by splinters or fragments of metal from field-gun and antitank shells, aerial bombs, mortars, land-mines and "booby" traps were called "shrapnel wounds," or "S.W."

Wounds having only a site of entry for the foreign body which was retained were called "penetrating."

Wounds having both sites of entry and exit were called "perforating."

Many patients had received more than one wound of the head, and often of different types; and others had received, in addition, wounds of other regions, of greater or lesser severity. The presence of "multiple" wounds and their complications must always be borne in mind when interpreting a patient's clinical condition in its true perspective.

TIME AND PLACE FOR TREATMENT

If a soldier with a wound of the head is unable to survive the first 12 hours, it is unlikely that he will live irrespective of what is done for him; thus, except in the case of meningeal hemorrhage or rapidly spreading subdural hematoma or severe arterial hemorrhage from the scalp, urgent surgical interference is rarely necessary. Adequate facilities and essential instruments, especially an electrosurgical unit and some form of suction apparatus, as well as a portable roentgenologic unit are necessary for dealing correctly with wounds of the head, especially those which involve the dura mater or deeper structures. Even if the medical officer dealing with them is not a fully trained neurosurgeon, he should at least be familiar with the technics employed in the care of damaged brain and in the control of intracranial bleeding, by the use of bulb syringes and warm saline, suction, silver clips, electrosurgery and muscle "stamps." He should also have a skilled assistant and anesthetist. These postulates have rarely been found at field ambulance dressing stations, even with attached field surgical units, or at casualty clearing stations under existing conditions, and with the number of medical personnel available up to the present.

Furthermore, apart from scalp and superficial skull toilet, hasty and often incomplete operations are best avoided, especially when the patient cannot be "held" for some days after the operation, for it has been proved frequently that although patients with severe head wounds stand transportation well before operation, they travel badly afterwards. Finally, it has been shown repeatedly that the time factor is not as important in dealing with head wounds as with wounds in other regions where the ideal time limit is set at 12 hours, or even less for abdominal wounds. This longer period of safety for head wounds had been fixed at 48 hours for civilian casualties during bombing raids on Great Britain in 1940–41, but in wounds from the Western Desert, for reasons already stated, successful excision, toilet, and closure, with a short period of drainage has been accomplished, frequently as late as 72 hours after wounding and in the following case, a period of ten days elapsed before adequate surgical attention was given:

Case 1.—Pvt. R. S. G., age 22, was wounded in the head on October 26, 1942, when a land-mine exploded near him. He did not lose consciousness but complained of some transient numbness of the left hand. He received extensive lacerated wounds of the scalp, in the right parietal region, with a hanging flap, exposing much bone.

There were also numerous other smaller scalp wounds nearby, posteriorly and towards the vertex. At a main dressing station, sulphanilamide powder and vaselined gauze were applied and he was hastily evacuated to an Australian general hospital about 90 miles in the rear, where he arrived early on October 27. Owing to the rush of casualties here, no operation was performed although roentgenograms taken that day showed a metal fragment of moderate size embedded in the skull just to the right of the vertex, with a small depressed fragment of bone indriven ahead of it. There were also several smaller extracranial fragments further posteriorly and laterally (Fig. 3). The wounds were dressed on several occasions, sulphonamides were continued by mouth, and he was evacuated by ambulance train to this Center, where he arrived late in the evening of November 3, 1942.

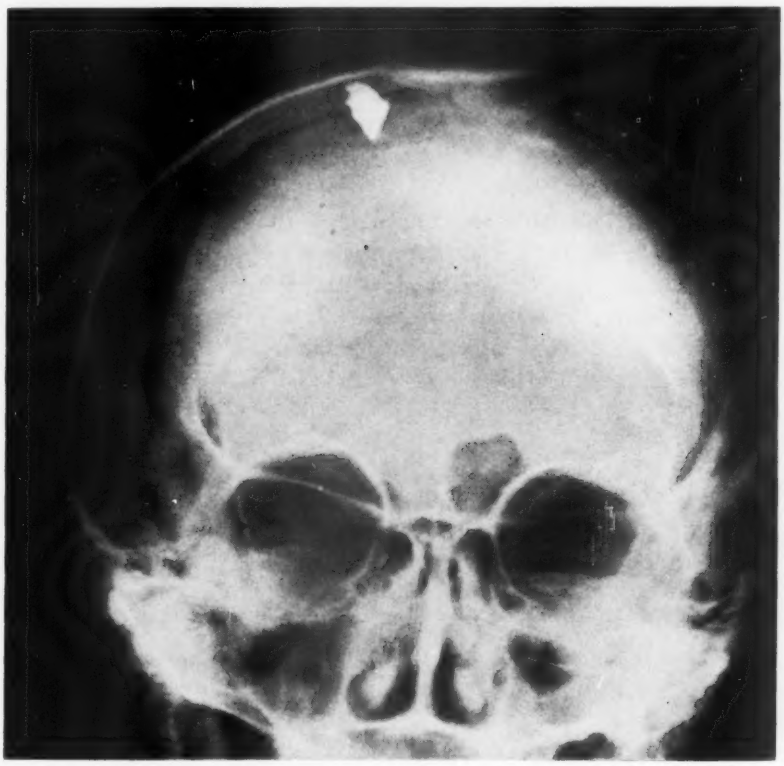


FIG. 3.—Case 1: Anteroposterior view, showing the irregularly-shaped metallic foreign body in the skull, near vertex, and to the right of the midline.

On examination, the patient looked ill. There was a foul smelling discharge from the extensive scalp wound. A portion of the loose scalp flap was necrotic, and much débris, dirt and hair could still be seen under its edges. The large foreign body was felt in a separate and smaller wound about three centimeters away. It was not so septic, and neither were the remaining small scalp wounds. At operation next day, under anesthesia with pentothal sodium given intravenously, the largest foreign body and small piece of indriven bone were removed with difficulty. The dura mater was intact and, after excision of the edges, this wound was sutured, without drainage. In a similar manner, the other small wounds were excised and closed. The large dirty wound was thoroughly washed out; all débris carefully removed, necrotic areas

of scalp excised down to the pericranium, and careful hemostasis secured. The fresh edges of the wound could only be partly approximated with silkworm gut sutures, leaving exposed an area of pericranium, about 3 x 2 cm. Complete closure was impossible owing to loss of scalp tissue, and, relieving incisions in the scalp being abhorred, a dressing of sulphanilamide powder and vaselined gauze was applied. This dressing was not disturbed for six days, and when removed, despite the onset of infective hepatitis on November 5, which had necessitated the suspension of sulphapyridine therapy by mouth, the closed wounds had healed and the raw area was covered with clean granulations. Secondary suture of this area was successfully accomplished by an undermining plastic procedure about three weeks later, when the jaundice had cleared up. He was discharged, with all wounds healed, to a convalescent depot on December 12, 1942, five weeks after arrival at this Center.

From the foregoing desiderata and statistics supplied personally by Major P. B. Ascroft, R.A.M.C., it has been shown in the treatment of head wounds that the best results were obtained by transporting all patients with other than minor head wounds back to some Special Center, (equipped and prepared to deal with and hold this class of case) preferably by aeroplane, as was done almost exclusively after the break-through by the Eighth British Army at El Alamein and by the Germans in their campaigns, even if it involved a delay of 72 hours, or more, until surgical measures were instituted. Having special Neurologic Centers in the forward areas was tried during the earlier desert campaigns, but was not found to be of much practical use at that time, owing to the difficulty of collecting and segregating head cases in forward areas and the lack of "holding" facilities.

THE OBJECTS OF TREATMENT

The objects to be aimed at in the treatment of head wounds are:

(1) To restore the injured structures as nearly as possible to normal, by the removal of destroyed tissues and of foreign bodies as soon as possible.

(2) To prevent complications which may lead to disability, deformity or death, by converting open wounds into closed, clean ones, when feasible.

(3) To return the soldier to his unit, in the shortest possible time, without the necessity of down-grading.

The complete attainment of these ideals is rarely practicable with battle casualties even at Special Centers, as will be realized from a consideration of the difficulties met with in this series.

GENERAL PROCEDURES AT SPECIAL CENTERS

Owing to its situation at the Base, and the long time taken for evacuation by ambulance trains and sometimes also by hospital ships, most of the patients in this series did not reach this Center until infection was already active, or else their wounds were healing. However, as a result of experience gained in the management of these wounds, mainly in their late stages, and from observations made at other Neurosurgical Centers, where the injuries were dealt with in a more recent state, a plan of treatment was evolved which proved effective for the conditions found in Middle East. A short description of the procedures advocated will now be given, followed by case

reports, selected to illustrate some of the complications and difficulties encountered.

As soon as the patient has been fed and rested after his journey, the hair is clipped short with fine cutting clippers all over the scalp, if not already done. This was found to be a most necessary step in order to remove all dirt and old blood, and to enable a careful inspection of the head to be made. Frequently the hair had only been hastily cut from the vicinity of the main wound and other smaller wounds had not been recognized.

Dressings are then inspected and the plan of treatment decided upon. Here, as at all subsequent dressings and inspections, every person present must wear an adequate surgical mask, covering the nose as well as the mouth. The "no-touch" (except with dressing forceps) technic of doing dressings must be adopted from the start, in order to reduce cross-infections to a minimum. As a guide for the future, if the wound is already infected and discharging, a swabbing is taken and an immediate smear and culture is made, to determine the predominating organisms (if any). Where sulphonamides had already been given in adequate dosage, cultures were frequently sterile. Complete and differential blood counts are also advisable to exclude anemia and postsulphonamide leukopenia. If satisfactory roentgenograms do not arrive with the patient, he is then sent to the Department of Radiology, with a request for anteroposterior, lateral and, occasionally, tangential exposures. Where indriven bone fragments and retained foreign bodies are suspected or found, stereoscopic views, taken with a Potter-Bucky diaphragm or Lysholm grid, are extremely helpful before attempting their removal. The importance of radiologic examinations of *all* battle wounds of the head, however slight, and even if consciousness has not been lost, has already been mentioned, and the mistakes which will otherwise be made, will be referred to again later.

If operation is decided upon, the whole head is then closely and carefully shaved by a *skilled* orderly with a *sharp* razor (both difficult to obtain and retain in the Army!). This is a very important step in eliminating infections and in enabling the postoperative and subsequent dressings to be adequately retained in place with a minimum of adhesive plaster. The scalp is painted with a 2% aqueous solution of iodine, after scrubbing with ethereal soap. If infection has not already developed in the scalp beyond the edges of the wound, local anesthesia, by the method of regional block, can be used with 1% ethocaine and adrenalin 1:200,000, in physiologic saline solution, after premedication with alopon (omnopon) gr. $\frac{1}{3}$ and scopolamine gr. $\frac{1}{150}$, given hypodermically an hour and a half beforehand. The alopon can be repeated half an hour before operation if necessary. In the presence of established infection in scalp or bone, or with a noncooperative nervous patient, general anesthesia is preferable by the administration of pentothal sodium intravenously, in 5% solution for induction and in weaker solution in saline or glucose-saline for maintenance. Fluids or blood should

be given intravenously during operation if the patient is dehydrated or anemic. In cases already infected and where streptococci, pneumococci, Friedlander's bacilli or anerobes predominate, an initial dose of four grams of sulphadiazine is given by mouth; or, if the patient is unable to swallow or has meningitis, three Gm. is given intravenously in a 30% solution. If the predominating organism is a staphylococcus, it is felt that a similar dose of sulphathiazole has more effect and less risk of producing complications. During the whole of the period under review, sulphadiazine was not always obtainable and then sulphapyridine had to be used, but the former drug was found to possess many advantages over the latter, due to its much lower toxicity and the greater concentration obtainable in the cerebrospinal fluid.

WOUNDS OF THE SCALP AND SKULL, WITHOUT DEPRESSION (GROUPS 1 AND 2)

In these groups some of the most serious and prolonged cases of morbidity were encountered, chiefly because, at the time of wounding, consciousness was not lost, and they were evacuated from the regimental aid post as "walking wounded, not serious," with just a first field dressing hastily applied. At the forward dressing stations and field surgical units, even frequently at casualty clearing stations in rush periods, there was no time to attend to them when more serious cases were waiting, and upon reaching a general hospital, as the wound was by now probably more than 36 hours old, proper excision and toilet were not carried out, under the mistaken idea that too much time had elapsed. In other instances, these wounds were received along with multiple wounds of a more serious nature and were given but scanty consideration until the appearance of sepsis called for more active measures.

Furthermore, it was often found necessary to "empty-out" general hospitals, close to the battle zone, in expectation of more casualties and, naturally, these cases were amongst the first to be transferred to other hospitals further back or even to convalescent depots "for dressings." Rarely had any roentgenologic examination been carried out, until some complication had occurred, and only then was some osseous lesion, with or without osteomylitis detected. Two instructive cases of this group are presented:

Case 2.—Pvt. F. G., age 26, was wounded, July 16, 1942, in the left parietal region when a bomb exploded. He never lost consciousness. The wound was dressed at an advanced dressing station four hours later, and he was passed on to a general hospital, where the dressing was changed but the wound was not excised or explored, although roentgenologic examination, July 18, showed that a piece of bone had been removed from the outer table of the skull in the left parietal region near the midline. Several foreign bodies were seen in the vicinity but no fracture through the inner table was detected.

On July 28, the wound was reported "clean and healing" and he was evacuated to this Center on July 30. The wound was then healing by granulation, and, with the assistance of eusol dressings, it had healed by August 8, and he was able to rejoin his training unit on August 20, 1942.

Soon afterwards the wound began to discharge. He was treated by his regimental medical officer until September 27, when he was referred to this Center com-

plaining of severe left-sided headache. A discharging wound was present in the left parietal area, near the vertex. Two days later the surrounding scalp became indurated and edematous, like a "Pott's puffy tumor." There were some swollen and tender lymphatic nodes in the left posterior triangle of the neck. Temperature 102° F. Without waiting for roentgenologic examination, he was operated upon, and a crucial incision was made to include the unhealed wound. The pericranium was raised up by pus from the underlying bare bone. Two bur holes were made in this bare area but no evidence of infection was found in the diplöe or extradurally. No foreign bodies were encountered. After insufflation of sulphanilamide powder, the wound was packed widely open with vaselined gauze, and sulphapyridine was administered by mouth in full dosage.

Although no further serious symptoms or complications occurred, healing by second intention took place very slowly and secondary suture never became practicable. A further roentgenologic examination, made November 3, showed a transradient area, close to the left parietal eminence, involving both tables of the bone, but not showing any evidence of active periostitis or osteomyelitis. One small foreign body was still present outside the skull.

He was last seen on December 14, when the wound had only just healed, but the scar was depressed, tender and adherent to the bone, and he was referred to a convalescent depot, for plastic operation later, if no further discharge occurred from the wound during the next two months.

Case 3.—Corp. K. M., age 37, was hit on the back of the head by a piece of falling rock from an explosion on April 17, 1942. He was only unconscious for a few minutes and was treated for a lacerated wound of the scalp "down to the bone" in the left occipital area at a field ambulance. He was later transferred to an Australian casualty clearing station, where, infection occurring in the wound, a roentgenologic examination of the skull was made, but no osseous lesion detected.

A few days later, he complained of very severe headache and facial neuralgia on the left side. He arrived at this hospital on April 27, with a dirty infected wound in the left occipital area, discharging freely. The surrounding scalp was tender and swollen but there was no "puffy tumor."

Hot fomentations were applied frequently, but, although the wound seemed to get cleaner, the headache and neuralgia became worse, with severe exacerbations, and the ocular fundi showed early papilledema. On May 8, a further roentgenologic examination showed an area of osteomyelitis near the lambdoid suture, with the presence of sequestra at the site of an old fracture. Operation was proceeded with at once. The scalp wound was excised and an area of necrotic bone with sequestra removed. An extradural abscess with thick pus was curetted off the underlying dura. The wound was sprayed with sulphanilamide powder, packed open with vaselined gauze and sulphanilamide administered by mouth in full dosage. Healing proceeded very slowly, and on July 7, it became necessary to remove further sequestra from the upper edge of the gap in the bone. This produced more headache and a severe reaction in the surrounding scalp. Sulphadiazine had just been received and was now given in full dosage with such good effect that the wound had healed by August 28, when he was returned to his unit symptom-free.

Many other cases were encountered where minor sepsis occurred in scalp wounds and delayed the patient's return to his unit for much longer than would have been necessary if healing had taken place promptly. An attempt should always be made, with these groups of wounds, to secure primary healing by a complete, yet not too extensive, excision of the wound and thorough mechanical cleansing of the damaged area. After spraying with sulphanilamide powder, the galea and skin should then be closed

separately by a double row of silk or linen thread sutures, around a small piece or pieces of corrugated rubber, for drainage. If the galea cannot be defined readily for suturing, one row of vertical mattress sutures may be employed instead.

If the edges of wound can not be drawn together without tension, even after triradiate extensions and undermining have been carried out, they should only be drawn together where possible, and the rest of the wound left open and packed with vaselined gauze, for plastic operation and secondary suture later. This procedure gives better results than attempting to obtain primary closure by making lateral relieving incisions and "sliding" the intermediate portions of the scalp across the defect.

Once sepsis had started, or if the wound broke down, then frequent applications of warm moist pads soaked in normal saline or eusol, until *complete* healing had occurred, were found most satisfactory. Any other methods, especially those which allowed a scab to form, under which pus could deceptively collect, only prolonged healing. Keeping the hairs close shaved right up to the edge of the wound was most essential.

The possibility of focal damage, often serious and permanent, being inflicted on the brain in these wounds, must always be borne in mind, especially where the impact has fallen tangentially. Such damage is usually the result of contusion and/or laceration of the brain, and does not call for exploration, unless signs of compression or massive hemorrhage are present too. The following case, in contrast with Cases 2 and 3, illustrates how rapidly scalp healing can occur, if correct, early treatment be given, and also what serious cerebral damage may underly a superficial wound:

Case 4.—Pvt. R. S., age 22, was wounded in the occipital region on July 11, 1942, by a splinter from a shell while wearing his steel helmet and sitting in a slit-trench. After a short period of unconsciousness, he remembered being carried away in an ambulance. At the regimental aid post, he was conscious, his wound was dressed, and he was evacuated direct to a general hospital, where he arrived 12 hours later. Here, a badly lacerated wound of the occipital region was excised, dusted with sulphanilamide powder, and sutured around a glove drain. No injury to the skull was detected at the time, nor at a roentgenologic examination made some days later.

On July 19, although the wound appeared to be healing satisfactorily, he became drowsy and restless alternately. Spinal puncture was performed and blood-stained xanthochromic cerebrospinal fluid, probably from a cerebral laceration, ran out at an initial pressure of 240 mm. The next day he was less drowsy and complained of deafness and defective vision. Examination of his fields of vision then revealed a right-sided hemianopia. On August 14, he was transferred to this Center. The wound in the scalp had healed completely but he still complained of visual difficulties, although his hearing was normal. Careful estimation of his fields of vision on the Bjerrum screen now showed bilateral lower nasal and temporal quadrantic defects, *i.e.*, he had a false horizon just below macular vision in each eye, (Fig. 4 a and b). Further investigations did not reveal the existence of any pressure effects from any space-consuming lesions, and the cerebrospinal fluid was now clear. He was sent to a convalescent depôt but when reexamined, October 15, the defects in the fields of vision were unaltered, and down-grading became necessary.

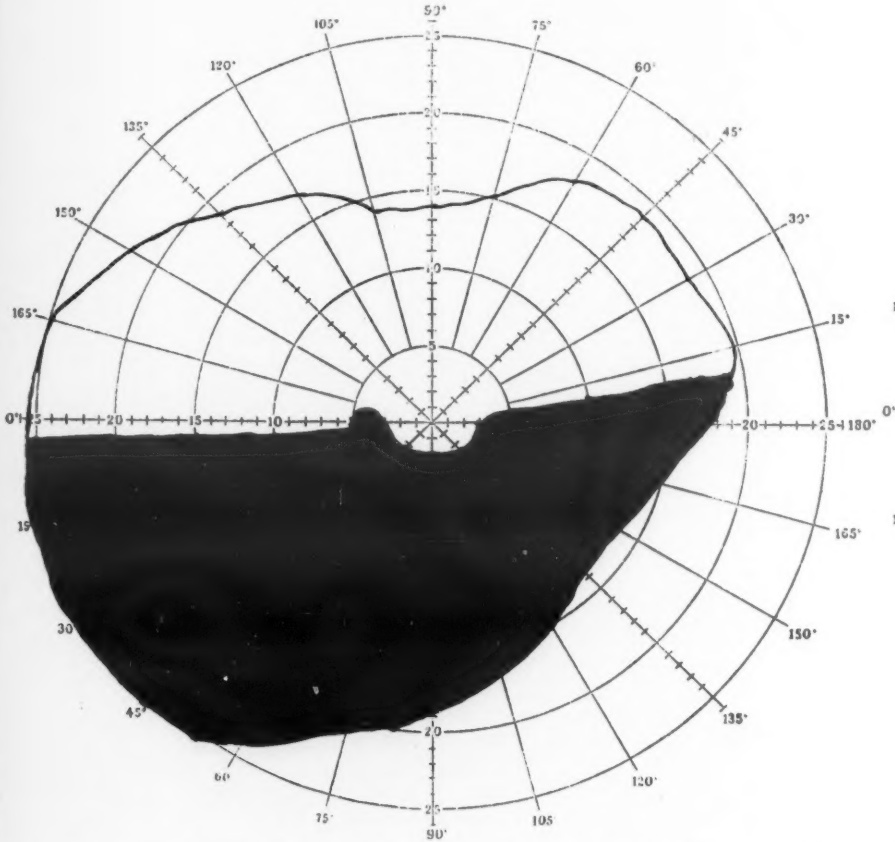


FIG. 4. (a)—Case 4: Field of Vision. Left eye showing false horizon just below macular vision.

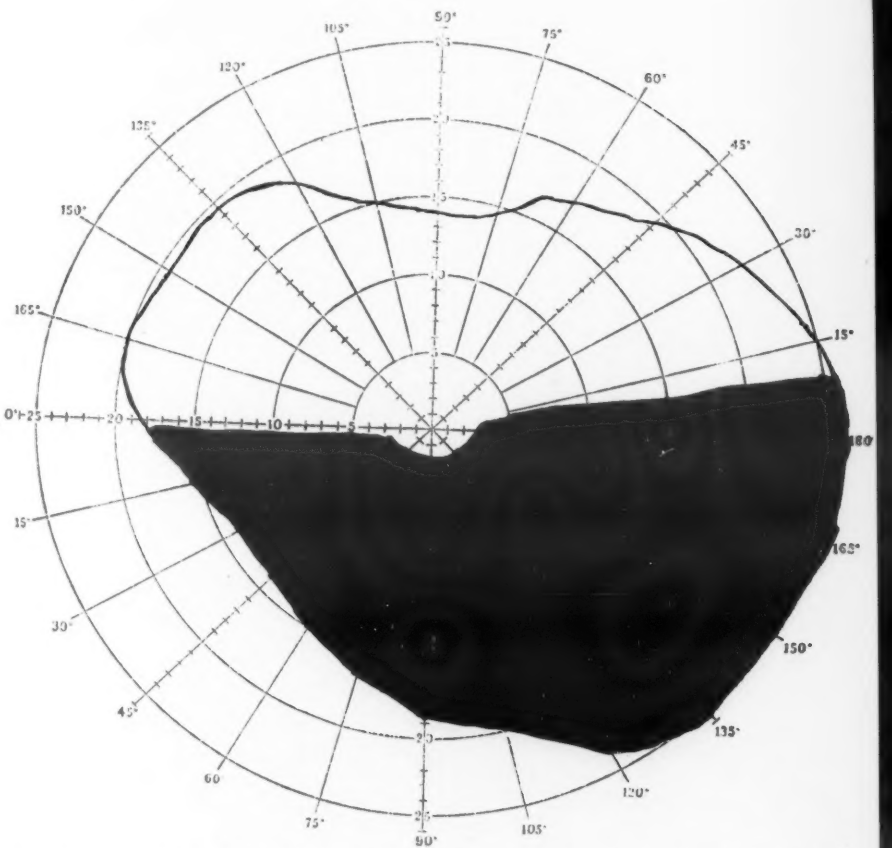


FIG. 4. (b)—Case 4: Field of Vision. Right eye showing false horizon just below macular vision.

WOUNDS OF THE SKULL WITH DEPRESSION BUT WITHOUT PENETRATION OF THE DURA (GROUP 3)

This group of wounds did not, as a rule, present any special problems. Included in it were cases of compound fissured fractures. In most instances there was more extensive involvement of the inner table than the outer table of the affected bone. The extent of these wounds was generally recognized at the first examination; consciousness had usually been lost for varying periods of time, and, being classified as severe, more attention was paid to them in the forward areas.

Careful surgical toilet and treatment, as early as possible, are necessary, however, if good results are to be obtained. Fissured fractures are rare but need thorough inspection for small retained foreign bodies, hairs and dirt between their edges and under the scalp. As in cases of Group 2, they may have areas of local brain damage deep to them, with focal neurologic signs. They do not warrant extensive craniotomy, but it is often advisable to make a bur hole in the line of the fissure to exclude extra- and subdural hemorrhage.

All loose and comminuted depressed fragments should be removed, and in most cases dirt, hair and débris are found to be associated with them. Special care is necessary in the removal of depressed fragments of bone near the midline, where the longitudinal sinus might be involved, and muscle "stamps" should always be prepared in readiness for the control of sinus bleeding during their removal. But it is remarkable how deeply fragments can be depressed, without penetrating the dura. Failure to recognize and adequately treat these cases was followed, however, by long periods of disablement and serious complications, as can be seen from the following case histories:

Case 5.—Lance Corp. G. R. J., age 22, of the Royal Tank Regt. received multiple "S. W.'s" of the head when a shell exploded as he opened the front of his tank on July 17, 1942. Loss of consciousness was of short duration. His wounds were dressed shortly afterwards at an Australian field ambulance. The following day, he arrived at a general hospital, where he was "held" for a week without any surgical treatment of his wounds. On July 25, he was transferred to another general hospital in the Canal Zone, and after 11 days there, reached a third general hospital in Palestine on August 4, 1942. He then complained of some headache on the left side, but his general condition was good. His wounds had healed except for one deep punctured wound in the left frontal region, in the floor of which pus could be seen pulsating. On August 8, his skull was examined roentgenologically for the first time, which demonstrated a comminuted fracture, with inward displacement of fragments of the inner table and a mottled appearance of the surrounding bone, suggesting osteomyelitis. Numerous small metallic foreign bodies were seen, some situated intracranially. There was also a small depressed fracture near the right parieto-occipital suture, but the wound in this region had healed.

On August 17, he was transferred to this Center. Two discharging sinuses were seen in the left frontal region and the depressed area of bone could be felt. The surrounding scalp was not edematous and its appearance did not indicate osteomyelitis. No abnormal neurologic signs were detected, although the patient complained of

occasional headaches and "giddy turns." Warm saline packs were applied to the discharging sinuses at frequent intervals until healing occurred, and on September 2, under local infiltration anesthesia, the depressed fragments of bone were elevated and removed. The surrounding bone was softened and vascular, from old osteomyelitis, but the dura mater was intact. The wound was left open and packed with vaselined gauze, and allowed to heal by granulation. This took about four weeks, and he was then transferred to a convalescent depôt. He was reexamined on November 25, 1942. Except for complaints of occasional slight headaches and "dizzy turns," he was free of symptoms. A small superficial metallic foreign body was removed from the scalp, the depressed scar was excised and the scalp reconstituted over this area by a plastic operation. The depressed fracture in the right parieto-occipital area was not causing any trouble and was left alone. Primary healing occurred after these operations and the soldier returned to his training unit on December 11, 1942.

The parlous and prolonged convalescence of the next patient showed the importance of removing fragments of bone as well as metallic foreign bodies if serious complications are to be avoided:

Case 6.—Pvt. A. P., age 21, received an "S. W." just above the nasion on September 1, 1942. He was unconscious for about eight hours, and thereafter mentally dull. He was evacuated late the same day from the main dressing station, with a large foreign body retained, and a note "no time for excision of wound" made on his field medical card. He reached an Australian general hospital on September 3, where the wound was dressed. Next morning, a roentgenologic examination showed a large foreign body embedded in the frontal bone, with some splintered bone fragments indriven by it for about two centimeters. On September 5, the foreign body only was removed, under local anesthesia. Improvement in his mental condition followed and he was evacuated to this Center, where he only arrived on September 10.

By that time, he was complaining of headache and had marked photophobia. The wound was discharging pus freely and some débris could be expressed. Both fundi showed early papilledema, but there was no neck rigidity or pyrexia. Sulphapyridine was given in full dosage and, on September 17, the wound was reopened and the depressed fragments of bone were removed. The dura mater appeared to be intact and there was no sign of extra- or intradural suppuration. The wound was packed with sulphanilamide powder and vaselined gauze, and allowed to heal by granulation.

About October 7, the patient complained of frontal headache and had some evening pyrexia. A few days later, relief followed discharge of pus from the wound but advanced papilledema, with recent hemorrhage, was observed in both fundi. Spinal puncture yielded slightly turbid cerebrospinal fluid, at a pressure of 230 mm., containing 320 cells per cu. mm., mainly lymphocytes. The protein content was 90 mg.%. A further course of sulphapyridine was commenced and some remission of symptoms and pyrexia followed. By October 25, although the wound had healed, the papilledema had increased, and a subdural or brain abscess was suspected. Small volume encephalography was performed by spinal puncture, with oxygen, but unfortunately no gas could be made to enter the ventricular system. Patent subarachnoid pathways were seen, however, over both frontal lobes. The cerebrospinal fluid then had 220 cells per cu. mm., mainly lymphocytes. The pressure was 440 mm. and the protein content was 50 mg.%. On November 20, the patient's condition had improved greatly; headaches were easier and the papilledema was subsiding. He was, thus, regarded as having had a condition similar to the so called "otitic or toxic hydrocephalus."

About three weeks later, a pulsating and inflamed swelling appeared at the site of the wound, and headaches, with pyrexia, recurred. Spinal puncture now yielded cerebrospinal fluid at a pressure of 450 mm., containing 110 cells per cu. mm. mainly

neutrophils. The protein content was 65 mg.%. On December 12, operation was again performed under local anesthesia. The scar was excised and a thick pulsating dura exposed and opened by endothermy. A brain needle was inserted into the left cerebrum and, at a depth of two centimeters, entered an abscess cavity through a very thick capsule. About ten cubic centimeters of thick yellow pus were evacuated, the needle was withdrawn, and the wound closed, after spraying with sulphathiazole. On culture, a pure growth of *Staphylococcus aureus* was obtained, and administration of sulphathiazole in full dosage was started by mouth. The wound healed primarily, and, on December 20, spinal puncture yielded clear cerebrospinal fluid, at a pressure of 220 mm., with a cell count of 75 neutrophils per cu. mm., and a protein content of 40 mg.%. Further aspiration of the abscess did not reveal any pus.

Early in January, 1943, however, headache and papilledema reappeared. Encephalography was repeated, but again no gas entered the ventricles and the cortical pathways were patent. The cerebrospinal fluid now only had 35 lymphocytes per cu. mm., although the pressure was still over 200 mm. On January 5, a brain needle with a silver cannula over it, was again inserted into the left cerebrum and through it, about 15 cc. of pus spurted out of an abscess cavity at a depth of about two centimeters. This was followed by blood-stained fluid. The cannula was left *in situ* and the needle removed. Once again, a *Staphylococcus aureus* was grown from the pus. Only a little blood-stained fluid drained subsequently from the cannula, and it was removed on the third postoperative day.

Thereafter, the soldier's condition improved greatly and his symptoms completely disappeared, although the papilledema was loath to subside. A final attempt to locate more pus was made on January 16, but, although the abscess capsule was felt and penetrated, none could be aspirated. By January 20, the optic fundi had subsided considerably but were not yet normal. The pressure of the cerebrospinal fluid at spinal puncture was still nearly 300 mm., though the fluid was crystal clear. As this Center had to close down, the patient was transferred to another Neurosurgical Unit in the Middle East. News of his future progress will be awaited with interest.

Fortunately, all wounds of this group do not cause such vicissitudes, as can be seen from the next case, which also demonstrated how the brain could escape damage despite considerable damage to the skull:

Case 7.—Pvt. H. T., age 26, received multiple "S. W.'s" in the right side of his head on October 25, 1942, without any period of unconsciousness. He was wearing his steel helmet at the time. After the application of a dressing, he was hurried back to an Australian general hospital. On October 28, a roentgenologic examination of the skull showed a comminuted, depressed fracture in the right parietal bone and two small foreign bodies stuck in the skull more posteriorly. Little was done at the time beyond changes of dressing as no abnormal neurologic symptoms or signs were present, and there was a big rush of more serious casualties. He was evacuated some days later, and arrived at this Center on November 3, with his multiple wounds mildly infected and discharging. After shaving and thoroughly cleaning the scalp, and the frequent application of hot saline fomentations for two weeks, the wounds had healed. Operation was performed on November 17, when the edges of the scar were excised, the depressed fragments of bone removed, and the wound closed with drainage, after spraying with sulphanilamide powder. The foreign bodies were not causing any symptoms and were not removed. Healing took place rapidly, so that the patient was discharged to a convalescent depot on November 25, and returned to his unit on December 14, 1942.

Depressed fractures in the temporal fossa differ from depressed fractures of bones of the cranial vault, and may not need surgical interference, unless there is evidence of middle meningeal or subdural hemorrhage associated with them. Apparently, the temporal muscle affords this area some protection and increased blood supply, which helps the fragments to overcome any infection introduced at the time of wounding. The following case illustrates these points:

Case 8.—Pvt. H. P., age 37, was wounded on September 1, 1942, in the right temporal region by a large piece of shell, which caused a long lacerated wound in the scalp and temporal muscle. The original notes were lost, but on arrival at an Australian general hospital on September 3, he was conscious, though drowsy and

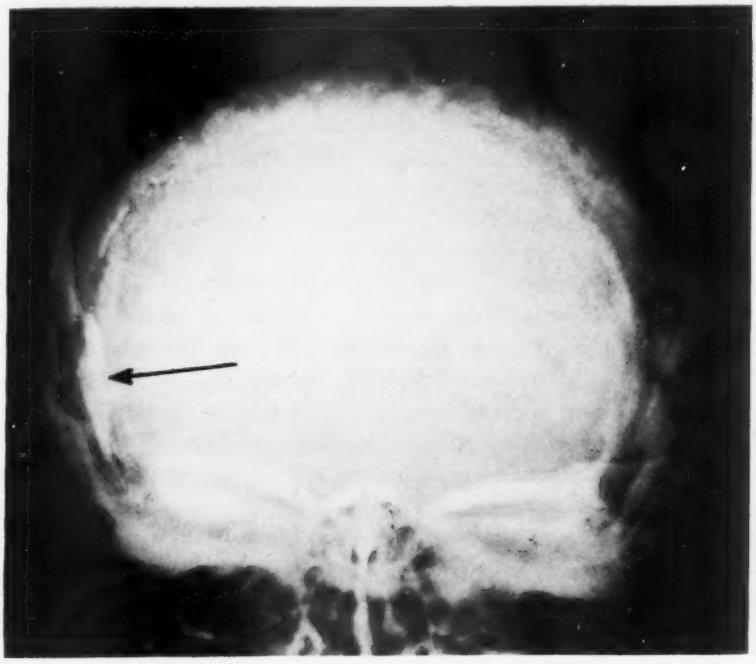


FIG. 5.—Case 8: Anteroposterior view, showing a large depressed fragment of the right temporal bone, but no evidence of osteomyelitis.

slow in answering questions. At times, he was confused and incoherent. There was a slight weakness in the left side of his face, but otherwise no abnormal neurologic findings. The edges of the wound had been excised but not sutured. Roentgenologic examination of his skull was carried out and the report was as follows: "A stellate fracture in the right temporal bone, extending into the middle fossa and upwards into the parietal bone; no displacement of fragments visible." By September 7, his mental condition had improved and the facial weakness had lessened. On arrival at this Center three days later, the wound was discharging freely. As underlying osteomyelitis was suspected, a further roentgenologic examination was made, which showed that a large fragment of the right squamous temporal bone was depressed (Fig. 5), but there was no sign of osteomyelitis. A few days later, a piece of latex rubber from the inside of his steel helmet came away, and thereafter healing proceeded

normally. No evidence of cerebral damage remained, and spinal puncture yielded clear cerebrospinal fluid under normal pressure, so that further surgical interference was not considered necessary.

PENETRATING AND PERFORATING WOUNDS OF THE SKULL (GROUPS 4, 5 AND 6)

These wounds are by far the most difficult to deal with and present many problems, largely due to the entry of bacteria through the protecting barrier of the dura mater. Any form of hasty or incomplete operation will only do more harm than good, and they, above all others, are best left alone until proper facilities for correct neurosurgical technic, controlled sulphanilamide therapy, and postoperative nursing are available, even if some delay results. The following methods of dealing with wounds of these groups were thus evolved:

Under anesthesia by local infiltration or pentothal sodium, a careful inspection of the wound or wounds, is made in the operating room, with the roentgenograms on a viewing box nearby. After a thorough skin preparation and excision of the edges of the wound, the extradural depressed fragments of bone are removed and the opening in the dura mater defined fully. To do this, it may be necessary to remove some undamaged bone. At the same time, hemorrhage from the dura is controlled.

Superficial débris, blood clot and destroyed brain are then gently washed away, by lavage and suction, from the track of the missile, usually with relief of intracranial tension and the return of pulsations in the area exposed. The number of indriven bone fragments has previously been counted and by careful exploration of the track of the missile and, with the help of the roentgenograms, they are then removed. It was surprising at times how deeply they had been driven in by even a small missile. The removal of all fragments is regarded as essential, and for this, a good headlight with adjustable focus, good suction, good retractors (or a Killain nasal speculum) and good assistance must be available. Frequently dirt, hair and other débris are found to have been taken in with them. On the other hand, it is considered only advisable to "go for" accessible metallic foreign bodies, as no abscesses or serious complications were encountered with retained metallic foreign bodies alone. With gentle technic very little bleeding need be caused by these procedures, and that can readily be controlled by endothermy or silver clips. The tracks are then filled with sulphathiazole or sulphadiazine cream, and in the absence of established infection, the opening in the dura mater is closed as securely as possible without causing undue tension. Only badly damaged and obviously necrotic portions of dura should be excised. Careful approximation of the edges of the tear in the dura mater is advocated wherever possible, to prevent hernia cerebri and leakage of cerebrospinal fluid. This precaution is particularly applicable, where the accessory nasal sinuses and mastoid air cells communicate with the wound, in order to prevent the development of cerebrospinal rhinorrhea and intracranial aerocoele. An unusual case with these and other complications, following a self-inflicted wound which involved the left orbit, frontal sinus and frontal regions is

being reported elsewhere (Money and Stoller, 1943, in press). Collaboration with an otorhinolaryngologist in these cases is advised.

Where the ventricular system has been penetrated or perforated by the foreign body, such closure is also desirable if an adequate toilet has been accomplished, but these wounds are so frequently fatal, that much experience in their treatment is hard to obtain. If cerebritis and/or brain abscess have already developed a soft rubber drain or narrow piece of corrugated rubber is inserted to the bottom of the track or abscess cavity and the dura closed around it. Then, after spraying with sulphathiazole or sulphanilamide powder, the scalp is closed around the drain. This drain is removed in 48–72 hours, if postoperative progress is satisfactory.

A prophylactic course of a sulphonamide by mouth is always commenced, or continued, if it has been started already. If meningitis and cerebritis were already established, then sulphadiazine was found to be the best drug, but it had to be given quickly and in large dozes, up to 18 Gm. by mouth or 12 Gm. intravenously, in each 24 hours, in order to maintain a concentration of over 10 mg.% of the drug in the cerebrospinal fluid for the next 72 hours. These estimations, carried out by colorimeteric methods, whenever cerebrospinal fluid is withdrawn at spinal puncture, are absolutely essential, for the correct regulation of the dosage of these drugs, as each patient absorbs and concentrates them at different rates and in different amounts. During the administration of such large doses of sulphonamide, it is necessary to give at least 3,000 cc. of fluids daily by mouth, with sufficient alkali to keep the urine alkaline, in order to avoid hematuria and anuria, which occur if the drugs become precipitated as crystals in the otherwise concentrated and acid urine. Under this regimen, these complications did not occur, although one fatal case of pontine hemorrhage was met with, but this appeared in an area of softening, about which, more will be said later. In unconscious patients, these drugs and fluids may have to be given with nasal feedings or intravenously. As a precaution again the production of blood dyscrasia and anemia, frequent blood counts and hemoglobin estimations should be made.

No experience was gained in the use of the electromagnet for the removal of metallic foreign bodies from the brain, as none was available; but as many of these foreign bodies are made of nonmagnetic metals, the use of this instrument is not considered worth while.

Postoperative dressings are done as infrequently as possible, provided the general condition of the patient is good and the wound is healing satisfactorily without much discharge. Adequate masking and the "no-touch technic" must be insisted upon, and it was found necessary to train nurses and orderlies especially in these methods. The appearance of a hernia cerebri or brain fungus calls for more frequent changes of dressing. Usually, the protruding brain is swabbed gently with a weak hypochlorite solution, sprayed with sulphathiazole powder and then covered with vaselined gauze. The intracranial pressure is reduced by spinal punctures, daily or as required.

Where there has been considerable loss or removal of bone from the

cranial vault, and where the wound has healed with a pulsating or depressed scar, adherent to the dura mater and brain cicatrix (especially in an area uncovered by thick hair), it is felt that bone grafting and plastic procedures are necessary, not only to relieve the usual complaints of local headaches, throbbing, giddiness on stooping, *etc.*, which remain, but also from a cosmetic and psychologic point of view, for these soldiers always imagine that should they receive a blow of any sort on the "unprotected" area of brain, fatal consequences are likely. With this series, however, no case has so far been followed-up long enough to see whether bone grafting were necessary, and no further mention of it will be made here, except to say, that, of recent years and after similar injuries in civilian life, insertion of portions of cadaver skull, after 20 minutes boiling, has proved both simple and satisfactory. Several cases have already been operated upon successfully, in this fashion, in Middle East at another Neurosurgical Unit (verbal communication from Major P. B. 9scroft, R.A.M.C.).

The following case histories are presented to illustrate many of these points:

Case 9.—Pvt. R. W., age 24, was blown off a motor cycle by the blast of a bomb, and sustained a wound in the middle of his forehead on September 12, 1942. After a short period of unconsciousness, he was confused and irritable when he reached a nearby South African field ambulance about two hours later. Operation was performed immediately, under general anesthesia. After toilet of the wound had been carried out, a comminuted depressed fracture, about the size of a shilling, was discovered, slightly to the left of the midfrontal line. On attempting to elevate the depressed area of bone, severe hemorrhage was encountered presumably from the sagittal sinus, and the wound had to be plugged with gauze. After insufflation of sulphanilamide powder and excision of the edges, the scalp wound was sutured over the gauze packing. The following day he was evacuated to an Australian general hospital, where, on September 14, the gauze packing was removed, without any further bleeding and the wound redressed.

He arrived at this Center on September 19. His wound appeared to be healing satisfactorily, but roentgenologic examination (the first) made shortly afterwards revealed several depressed fragments of bone, deeply indriven. As no abnormal neurologic signs were present, the wound was allowed to heal, and on October 13, under anesthesia with pentothal sodium, it was reopened and the indriven fragments of bone removed, without encountering any severe hemorrhage. Portion of the posterior wall of the left frontal sinus was involved and had to be removed, but the mucous membrane was intact. The deepest fragment had penetrated the dura mater to the side of the sagittal sinus. No signs of sepsis were found, so the wound was closed, and healed by first intention, with the aid of a short prophylactic course of sulphadiazine.

In this case, it appeared that the early surgical toilet and closure of the wound after excision, eliminated infection and complications, although the bone fragments could not be dealt with at the time.

The wound of the next patient also received prompt attention and healed primarily with the aid of sulphadiazine despite the retention of some indriven bone débris. Owing to its extremely inaccessible site, the question of removal of this metallic foreign body never arose. It was amazing what little serious damage it had caused considering the regions of the brain it had traversed.

Case 10.—Pvt. A. W., age 27, received a severe penetrating "S. W." of head, at about 1700 hours on September 19, 1942, when a shell exploded in the dugout he was occupying. He was not wearing his steel helmet at the time. Consciousness was lost at once but regained later at the regimental aid post, where a lacerated wound of the scalp was dressed. His left pupil was dilated and the plantar reflexes in both feet were "extensor" at the time. At midnight September 29, operation was performed at a casualty clearing station. A small wound near the bregma was explored, and a hole found in the skull over the superior longitudinal sinus. Some indriven spicules of bone were removed and there followed severe bleeding, which was controlled temporarily with gauze packing. After excision of its edges and a liberal insufflation of powdered sulphanilamide, the scalp wound was closed around two corrugated rubber drains. He was evacuated next day by air ambulance to a Neurosurgical Center in Egypt, where he arrived in a restless and semiconscious condition. There was paresis of the left arm and leg and the head and eyes were turned to the left. The left pupil was still larger than the right, and the left abdominal reflex was absent. Pyrexia and signs of meningitis were absent.

On September 2, the drains were removed and some serous discharge was observed. At 1800 hours, four Gm. of sulphadiazine were given intravenously. Soon afterwards an attack of renal colic and hematuria occurred, so that no more of this drug could be given. The next day the sutures were removed. The edges of the wound appeared to be softening and bulging, and it looked as if an hernia cerebri were developing. Spinal puncture yielded blood-stained cerebrospinal fluid at a pressure of 180 mm., with a protein content of only 20 mg.%, and containing 5.5 mg.% of sulphadiazine. The wound looked better after withdrawal of sufficient fluid to bring the pressure down to 120 mm.

On September 25, the first roentgenologic examination of the skull was made, which showed "a small defect in the midline 2.5 cm. posterior to the bregma, with some bone débris indriven for about 3 cm. and a metallic foreign body with a diameter of 0.5 cm. lying just to the right and behind the sella turcica." No further active treatment was undertaken, and by September 27, the wound had healed satisfactorily. The left pupil was still larger than the right but both reacted to light and accommodation. Diminution of sensation to pin-prick was noted in the areas of skin supplied by the 2nd and 3rd divisions of the right trigeminal nerve, and the left hemiplegia persisted; flaccid and hypotonic in the upper limb but more spastic in the lower limb where the tendon reflexes were exaggerated and the plantar response was "extensor."

Encephalography was performed on October 7, and the presence of any space consuming lesion was excluded. Thereafter, the patient became more alert, and as voluntary power returned in his left lower limb he was able to walk with assistance. as it was unlikely that he would become an efficient soldier again for at least a year, he was repatriated from Middle East early in December, 1942. The hemiplegia was still improving and no other symptoms were present.

Another patient had a single large retained metallic foreign body. It was not causing any symptoms, but the involvement of the sensorimotor area and its relative accessibility seemed to indicate the necessity for its removal, which was accomplished without incident and without finding any sepsis.

Case 11.—Tpr. T. G., age 22, of the Royal Tank Regiment was wounded in the left parietal region on October 25, when his tank was attacked by a dive-bomber. A piece of bomb perforated his steel helmet, which he was wearing at the time. Loss of consciousness was only momentary. He remembered seeing a flash, and later, noticed that he could not control or stop moving his right hand. In it was a feeling

of "pins and needles," as if it were electrified, and when one of his mates touched his steel helmet at the site of the perforation he felt a "shock" in his right hand. This indicated that the sensorimotor area corresponding to the right hand had been damaged. His evacuation through a light field ambulance and an Australian casualty clearing station was rapid, with merely changes of dressing without roentgenologic examination or operation. On October 27, at a general hospital, a cock-up splint was applied to his right wrist on account of weakness in dorsiflexion. By November 7, when transferred to another general hospital in Palestine, the wound in his scalp had almost healed, and except for slight clumsiness on skilled movements, the right hand had recovered its power, and sensations were normal. Roentgenologic examination was first made on November 19, which revealed "a punctured fracture in the left parietal bone, with a metallic foreign body in the underlying brain."

He was then sent to this Center, where removal of the foreign body and some depressed pieces of bone was carried out under local infiltration anesthesia. No evidence of infection was encountered and the wound healed by first intention. Lumbar puncture was performed early in January, 1943, when he returned from a convalescent depôt for review. The intracranial pressure was normal and the cerebrospinal fluid quite clear. The right hand seemed normal in every way. His complaints of headaches, as the day wore on, were accounted for by an advanced grade of myopia, for which glasses had been ordered. He was considered to be fit for return to his unit, when they were supplied. There did not seem to be any indication for encephalography.

The next case had a somewhat similar injury, but a more parlous convalescence with probably some permanent disablement.

Case 12.—Pvt. H. P., age 26, of the Gordon Highlanders, was rendered unconscious by a mortar bomb at 0100 hours on the morning of October 24, 1942. He regained consciousness at 0440 hours, and applied his own field dressing to a wound of his scalp. He crawled back alone to safety and lay there till found at noon next day. He was evacuated rapidly down the line, arriving at a general hospital on October 26, where he complained of intense headache. A superficial scalp wound in the right frontal region was dressed after removal of some matted hair. On October 28, he was transferred to another general hospital in Palestine. On arrival there, on October 30, his headache was still severe. Neck rigidity was present and Kernig's sign was positive. Temperature 99.4° F., pulse 60. Roentgenologic examination of the skull revealed (Figs. 6 and 7) a gap in the cranial vault through which a minute foreign body had traveled and lodged deep in the right frontal lobe. Several loose pieces of bone were present in the brain along the track of the foreign body.

Spinal puncture was performed and clear fluid was obtained, not under pressure, and removal of 5 cc. relieved the headache. No record of any bacteriologic or cytologic examination was found. The wound was packed with sulphanilamide powder, and 2 Gm. of sulphanilamide were given, by mouth, every four hours. The next day pyrexia was slightly higher, and, although the headache was less, the patient was drowsy. He was then transferred to this Center and on arrival, at 1800 hours, the wound was seen to be bady infected, with a foul purulent discharge, admixed with gas, from which hemolytic streptococci were grown on culture. Obvious signs of meningitis were present. Spinal puncture yielded yellow fluid, at a pressure of 200 mm., containing 520 neutrophils and 320 lymphocytes per cu. mm. The protein content was 185 mg.%. Three Gm. sulphadiazine were given intravenously, and he was allowed a good rest after his journey.

On November 1, he was better, and the temperature had fallen to normal. Spinal puncture was repeated and yielded clear fluid, at a pressure of 150 mm., containing

200 neutrophils and 475 lymphocytes per cu. mm. The protein content had fallen to 85 mg.%. The sulphadiazine content of the cerebrospinal fluid was only 6 mg.%, so a further three Gm. were given intravenously and repeated 12 hours later.

On November 2, the signs of meningitis had disappeared but as the discharge from the wound was still copious and foul, operation was proceeded with, under anesthesia with pentothal sodium. The edges of the wound in the scalp were excised

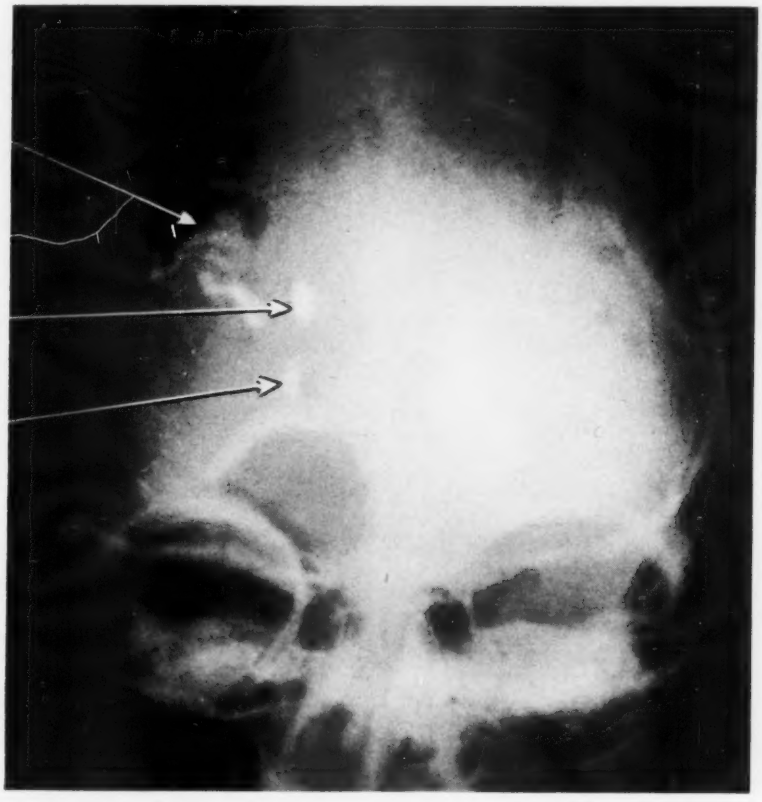


FIG. 6.—Case 12: Anteroposterior view, showing the irregular gap in the right frontal bone, and the numerous irregular pieces of indriven bone. The small metallic foreign body is situated most inferiorly toward the midline.

and the hole in the bone enlarged, to define the tear in the dura mater. It was blocked by a piece of indriven bone, and when this was removed, pus and gas escaped from a brain abscess, with relief of intracranial tension. The cavity of the abscess was explored and three more fragments of indriven bone and much necrotic débris were removed. The deepest fragment was 7 cm. from the level of the dura and must have been very close to the lateral ventricle. The small metallic foreign body was not found. The cavity was irrigated, and a small soft tube inserted into its depths. The wound was sprayed with sulphanilamide powder and closed around the tube. A pure culture of hemolytic streptococci was grown from the pus of the abscess. As soon as the patient became conscious the administration of sulphadiazine was commenced by mouth, four Gm. as an initial dose followed by two Gm. every four hours.

The next day, his condition was satisfactory, and the sulphadiazine content of his cerebrospinal fluid had reached 12.5 mg.%. Convalescence was thereafter uninterrupted;

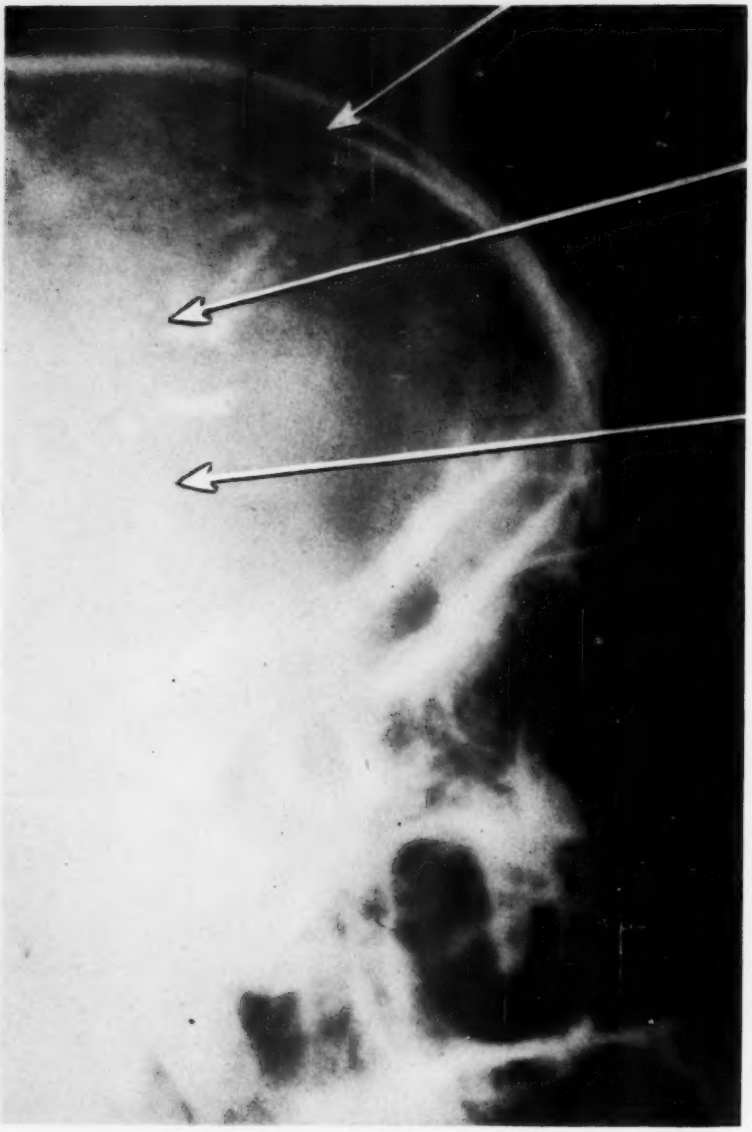


FIG. 7.—Case 12: Lateral view, again showing the irregular gap in the cranial vault and the indriven bone fragments along the track of the small missile, which is the most inferior and posterior foreign body.

the tube was removed on November 8, and sulphadiazine was stopped after a total amount of 64 Gm. had been given.

By December 8, the abscess cavity had completely healed and he was sent to a convalescent depôt. He returned for review early in January, 1943, feeling well except for headaches on exertion and giddiness on stooping down. The scar in the scalp, at the side of the wound, was indrawn, somewhat tender, and pulsated during exertion. Encephalography was performed by the spinal route. The pressure of the cerebrospinal fluid was normal; it only contained two lymphocytes per cu. mm.,

and the protein content was 30 mg.%. Roentgenologic examination after the introduction of 30 cc. of oxygen showed some generalized enlargement of both lateral ventricles in their anterior horns, with a definite "wandering" of the right anterior horn towards the cicatrix resulting from the abscess. The metallic foreign body previously seen had now separated into two parts, and both pieces were more superficial.

The patient was returned to the convalescent depôt for further graduated training, but it was thought that bone grafting would be necessary later, and that he would probably not be fit to return to front line duties.

The fifth case selected from these groups was the only one of the series in which a fatality occurred, and demonstrated how serious infections of the wounded brain can still be, once they reach a ventricle, despite the advent of the sulphonamides. Unfortunately, this case was one of the earliest in the series and was treated before a colorimeter was available and before the importance of determining the concentration of sulphadiazine in the cerebrospinal fluid of each patient (irrespective of dosage) was realized. Had this case been encountered later on, larger doses of sulphadiazine would have been given for a longer time in the first course, and operation for the removal of the remaining indriven bone fragments would have been undertaken much sooner. Full details, with the findings of the postmortem examination are submitted.

Case 13.—W. O. (Class 2) : E. W. H., aged 33, of the N. Z. E. F., was admitted to a New Zealand field ambulance on July 8, 1942, with a history of having received a "S. W." of head in the right occipital region 14 hours previously. Loss of consciousness was not recorded. The wound was cleaned with peroxide of hydrogen and dusted with sulphanilamide powder. He reached a general hospital next day where his wound was redressed. An entry on his field medical card stated "Not considered suitable for surgery. Skull does not appear to have been fractured. No roentgenograms taken."

On July 10, he was transferred to another general hospital in the Canal Zone, where a roentgenologic examination revealed a comminuted fracture in the right occipital region. Despite complaints of constant headaches, no surgical measures were instituted, as the wound was healing satisfactorily with daily dressings.

On July 24, he was evacuated by ambulance train to a general hospital in Palestine. Apart from headaches, his condition seemed good and the wound had almost healed. On July 30, his headache had become severe enough to warrant relief with morphia, and vomiting began. His temperature was elevated and total white cell count was 16,000 per cu. mm. Roentgenologic examination showed "an area of bone necrosis in the right occipital region, ovoid in shape, and about 4 x 2.5 cm." Spinal puncture, performed next morning, yielded cloudy fluid, under pressure, containing 19,000 cells per cu. mm. Hemolytic streptococci were grown from it, on culture. The administration of sulphapyridine in full dosage was commenced at once by mouth.

On August 1, his condition was critical, and his temperature had reached 105° F. Under anesthesia with pentothal sodium, the wound was explored and several depressed fragments of bone found. Some of them had punctured the dura mater, and on attempting to dislodge one of them severe bleeding began, probably from the lateral sinus. This fragment was removed and the bleeding was controlled by plugging with gauze. The exposed dura was then needled and some pus was aspirated at a depth of about two centimeters. Hemolytic streptococci were also grown from this pus. After dusting with sulphanilamide powder, the wound was packed with vaselined gauze, and the administration of sulphapyridine continued by mouth.

During the next few days his condition improved somewhat and, on August 6 he was transferred to this Center. On admission, he complained of bilateral headache and nausea. There was marked rigidity of his neck. The abdominal reflexes were absent and a left-sided homonymous hemianopia was detected but no papilledema. Spinal puncture yielded turbid, yellowish fluid, at a pressure of 240 mm., containing 780 cells per cu. mm. It was sterile on culture, but the protein content was high, *viz.*, 250 mg.%. The wound looked clean and was healing by granulation. A reexamination of the right occipital region, roentgenologically, showed (Fig. 8) "an old comminuted fracture, extending across the lambdoid suture into the mastoid region. Some fragments of bone are still remaining, in the lower part of the opening and probably displaced inwards." In view of the failure of the sulphapyridine to clear up the meningitis, sulphadiazine was substituted, two Gm. by mouth every four hours.

On August 10, he was better clinically, although spinal puncture yielded fluid, still slightly yellowish and turbid, at a pressure of 290 mm. The cell count had fallen to 265 cells per cu. mm., but the protein content had risen to 400 mg.%. (In the light of postmortem findings, it is believed that this indicated that ependymitis and pyocephalus were already present at that time). As 40 Gm. of sulphadiazine had been given, its administration was suspended.

On August 13, spinal puncture showed that, whereas the pressure of the cerebrospinal fluid was lower at 270 mm., the cell count had risen to 760 per cu. mm. The protein content was 350 mg.%. A second course of sulphadiazine was commenced by mouth; four Gm. were given every six hours for four doses, followed by two Gm. every four hours. Under local anesthesia, the wound was explored. Two pieces of loose bone were located deep to the dura and were surrounded by granulation tissue, but their removal caused profuse bleeding from the lateral sinus and further exploration could not be proceeded with.

Some improvement took place during the next few days and the sulphadiazine was again suspended, on August 17, after 38 Gm. had been given. Three days later, however, intense headaches and vomiting returned. The patient became irrational, facile and slightly aphasic. Weakness and incoordination in the left upper and lower limbs were found, and the plantar reflex was "extensor." Bilateral grasping reflexes were present. Spinal puncture yielded slightly turbid yellow fluid, at a pressure of 440 mm., containing 580 cells per cu. mm., and 700 mg.% of protein! Roentgenologic examination was repeated, and two loose pieces of bone were still inside the cranium and deep to the posterior end of the wound. It was presumed that an abscess had formed in the right cerebral hemisphere, and was extending forward to involve the internal capsule and the lateral ventricle. Accordingly, under local anesthesia, the wound was again explored, and the two pieces of indriven bone were removed from the occipital lobe, at a depth of about three centimeters, followed by a small amount of blood-stained purulent discharge. A bur hole was then made 6 cm. above the inion and 3 cm. to the right of the midline; and the right cerebrum explored through it with a brain needle. The right lateral ventricle could not be located, and no abscess was found in the parietal or temporal lobes, but, in the direction of the wound, at a depth of 5 cm., a nonencapsulated abscess was located. There drained from the needle about 10 cc. of pus, from which colonies of streptococci and staphylococci were grown. The patient's condition had improved slightly at the end of this procedure and on return to the ward, a third course of sulphadiazine was started with an initial dose of four Gm., followed by three Gm. every six hours in nasal feedings.

By August 28, further improvement had occurred, especially in his mental condition. Headaches and neck rigidity were less, and he had been apyrexial for 48 hours. Spinal puncture yielded clear fluid, at a pressure of 240 mm., containing only 85 cells per cu. mm. The protein content had fallen to 190 mg.%. The wound looked

clean, and there was no hernia cerebri. A brain needle was introduced into the right occipital lobe but only a little old blood was evacuated. It really looked as though the infection had been overcome at last; and next day, after 77 Gm. had been given, the third course of sulphadiazine was stopped.

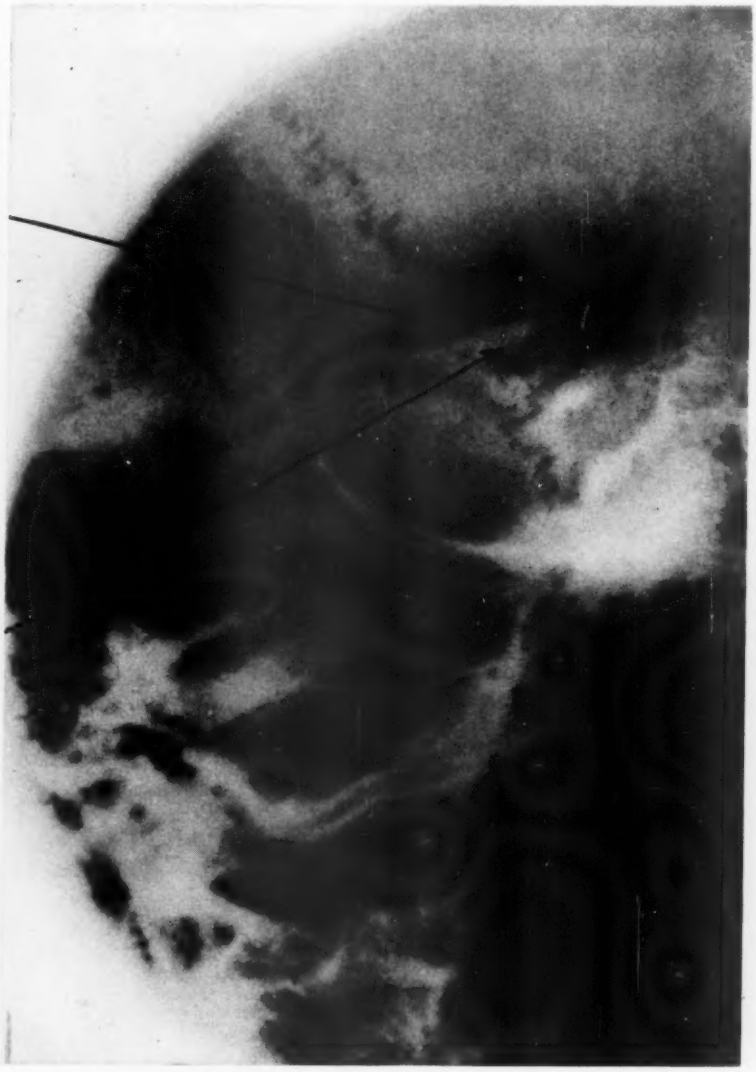


FIG. 8.—Case 13: Oblique view of right occipitomastoid region, showing the gap in the bone caused by the missile and the line of the fracture, with fragments of bone still present and probably indriven in the lower part of the opening.

This happy state of affairs was, however, shortlived and on August 31, a sudden relapse occurred. The patient became deeply unconscious, with dilatation of both pupils, and left-sided hemiplegia. Patellar and ankle clonus was elicited, and the plantar responses were "extensor" on both sides. A brain needle was passed through the bur hole and about 10 cc. of serosanguineous pus were released from the occipital lobe, and

a further 10 cc. of yellow pus at a depth of 7 cm. from the temporal lobe, possibly from the lateral ventricle. After a temporary improvement, his condition rapidly deteriorated, and he died in a state of hyperthermia late that night.

A postmortem examination of the head was made next day by Major E. B. Jones, the pathologist to the Hospital. He found some infected brain tissue extruding from the wound in the right occipital region. The right lateral sinus had been opened by

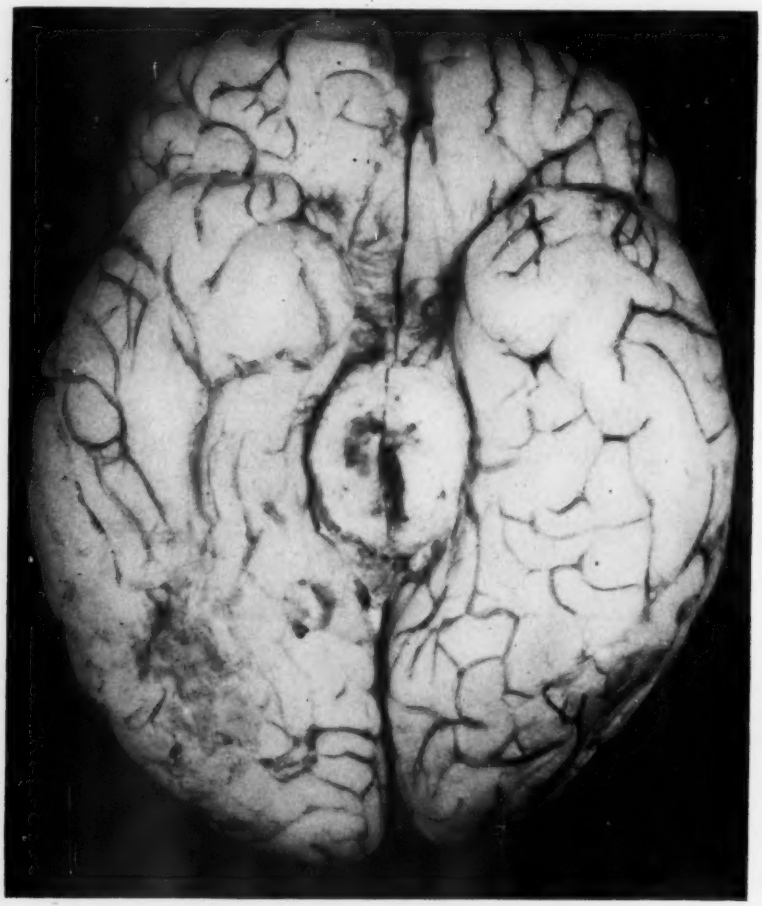


FIG. 9.—Case 13: The midbrain has been cut through just where it joins the pons. The section on the right side is at a slightly higher level than on the left side. The undersurface of both cerebral hemispheres can be seen. Note the area of traumatic cerebritis in the right occipital lobe, and the softening and hemorrhage in the pons and midbrain.

the wound and its lumen had been obliterated by organized blood clot. An area of traumatic cerebritis was seen where the right occipital lobe was adherent to the edges of the tear in the dura mater at the site of the original wound (Fig. 9). The fore- and midbrain were removed by cutting through the upper part of the pons, and an extensive area of softening was revealed in the midbrain and pons, in which a recent hemorrhage had occurred (Figs. 9 and 10). The tentorium cerebelli and the rest of the brain were normal. Signs of chronic meningitis were present in the posterior fossa. The brain was then placed in formol-saline solution and, ten days later, horizontal sections were made, at intervals of 1.5 cm., through the cerebral hemispheres (Figs. 10

and 11). From the site of trauma in the posterolateral aspect of the right occipital lobe, and passing forwards and upwards till it reached the right lateral ventricle, was an area of softened brain tissue, in which hemorrhages had occurred and several abscesses had formed. The hemorrhages had apparently occurred at different times, some showing yellow discoloration. The right lateral ventricle was filled with material which looked like coagulated cerebrospinal fluid, mixed with organized pus, indicating

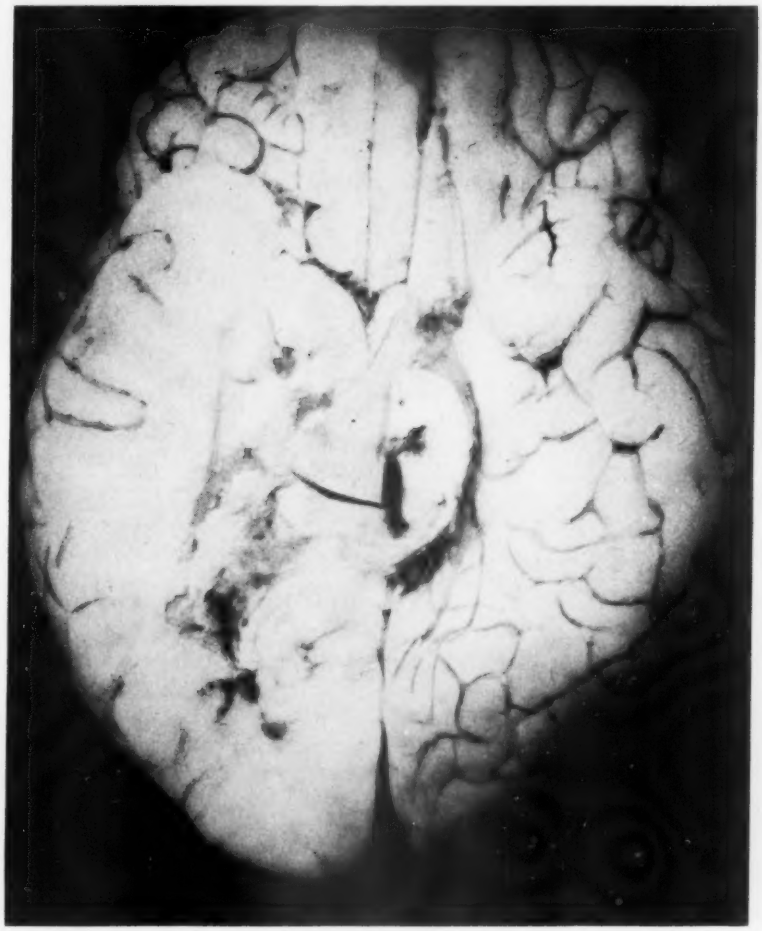


FIG. 10.—Case 13: Horizontal section through the right cerebral hemisphere at a depth of 1.5 cm. from the undersurface, photographed from below. Note the area of softened brain extending from the right occipital lobe to involve the lateral ventricle. It contains many small hemorrhages and abscesses.

localized pyocephalus of some duration. The right cerebral hemisphere was much larger than the left and had been dislocated across the middle line. This had interfered with the emptying of the left lateral ventricle, which was considerably enlarged and filled with clear fluid. The third and fourth ventricles were also filled with clear fluid; and thus, the pyocephalus in the right lateral ventricle must have shut off and was apparently proceeding to a stage of cure (such was the power of the sulphadiazine!) when the fatal pontine softening and hemorrhage occurred. No reason for this final complication can be offered, as neither the original wound or subsequent operative procedures involved

this region, and repeated blood examinations during the administration of the large doses of sulphonamides had not revealed any blood dyscrasia.

The last case is presented to show that sepsis, and even an abscess, may lie latent around a piece of indriven bone, without symptoms and without signs of increased intracranial pressure; another cogent reason for the removal of organic foreign bodies.

Case 14.—Pvt. A. H., age 31, received a severe "S. W." of head with indriven bone fragments in the right parieto-occipital region, at 1000 hours, on July 24, 1942. He was wearing his steel helmet. He was only unconscious for a few minutes, and complained of blurred vision when he regained consciousness. Operation was performed at a casualty clearing station, at 1800 hours, next day. The edges of the wound were excised, some pulped brain and superficial bone fragments removed, and the wound closed in two layers around a glove drain, after dusting with sulphanilamide. He was evacuated the same day to a general hospital where a course of sulphapyridine was commenced by mouth. Healing of the wound progressed satisfactorily but a roentgenologic examination, made on July 28, showed an annular area of bone missing from the right posterior parietal area, with a collection of indriven bone fragments deep to it.

It was realized that their removal was indicated, and he was transferred to a Neurosurgical Unit in Egypt on July 31. There were no abnormal signs detected on neurologic examination except a left homonymous hemianopia. During the next three weeks, the wound discharged some old blood clot and leaked a little cerebrospinal fluid on and off, but by August 22, it had healed except for a small button of granulation tissue. Routine encephalography was performed and showed a filling defect in the posterior horn of the right lateral ventricle. The cerebrospinal fluid, though clear, had five polymorphs per cu. mm., and the protein content was 40 mg.%.

It, thus, appeared to Maj. P. E. Ascroft, R. A. M. C., that the patient had a brain abscess, despite his satisfactory clinical condition, and on August 26, the wound was reopened, and the "track" in the brain was explored. Pus was encountered at a depth of 2.5 cm. from a thick-walled abscess at this site, seven irregularly-shaped pieces of bone, up to two centimeters in length, were removed. Sulphathiazole cream was injected into the cavity, and the wound closed around a rubber drain. On culture of the pus, a staphylococcus was grown.

Convalescence was uneventful and, on September 7, he was transferred to this Center for down-grading, due to the persistence of the left homonymous hemianopia, before a final set of steroscopic roentgenograms, taken on September 6, had been examined. These revealed seven or eight more pieces of indriven bone of various sizes; and the presence of another residual abscess had to be considered. Spinal punctures, on September 16 and 24, yielded clear cerebrospinal fluid, at normal pressure, only containing a few lymphocytes per cu. mm.; but the protein content of 50 mg.%, on each occasion, indicated the persistence of a focus of infection. Accordingly on October 3, the wound was reopened, the scar in the dura mater defined, and the region of the old abscess explored. With great difficulty, five separate pieces of indriven bone were removed from depths varying between 3 and 5 cm., and around one of them a small amount of pus was found in an abscess cavity which was removed by suction. The wound was closed with drainage, after the insufflation of sulphanilamide powder. A pure culture of staphylococcus was again grown from the pus.

About three days later, symptoms and signs of meningitis appeared, despite a prophylactic course of sulphapyridine, but this infection gradually subsided with

increased dosage of this drug, and a series of spinal punctures. On November 6, examination by Maj. J. Kingsley, the ophthalmologist to the Hospital, showed normal fundi but a complete left homonymous hemianopia (see Charts, Figs. 12 a and b). Spinal puncture yielded clear fluid under normal pressure, with 15 lymphocytes per cu. mm., and a protein content of 45 mg.% Stereoscopic roentgenograms were again taken, and showed three indriven fragments of bone still *in situ*, but it was decided

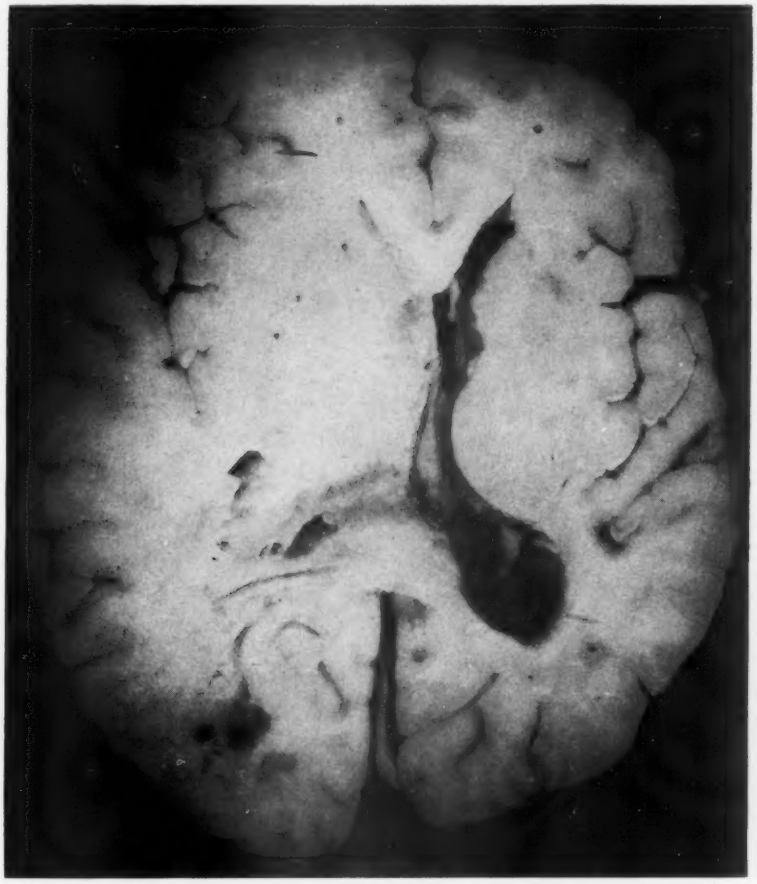


FIG. 11.—Case 13: Horizontal section through both cerebral hemispheres, at a depth of 3 cm. from the undersurface, photographed from below. Note the large size of the right cerebral hemisphere compared with the left; also the right lateral ventricle filled with congealed and organized cerebrospinal fluid and pus. The left lateral ventricle is enlarged but not infected.

to leave them there for the time being rather than risk stirring up another attack of meningitis, and he was sent to a convalescent depot for a month. His condition remained very satisfactory during that time, and he was repatriated after down-grading about the middle of December, 1942.

So far, little has been said about wounds of Groups 5 and 6, *i.e.*, perforating or "through-and-through" wounds, and penetrating wounds, where the missile has entered through the orbit and/or accessory nasal sinuses. Usually, there were greater degrees of neurologic disturbance and loss of

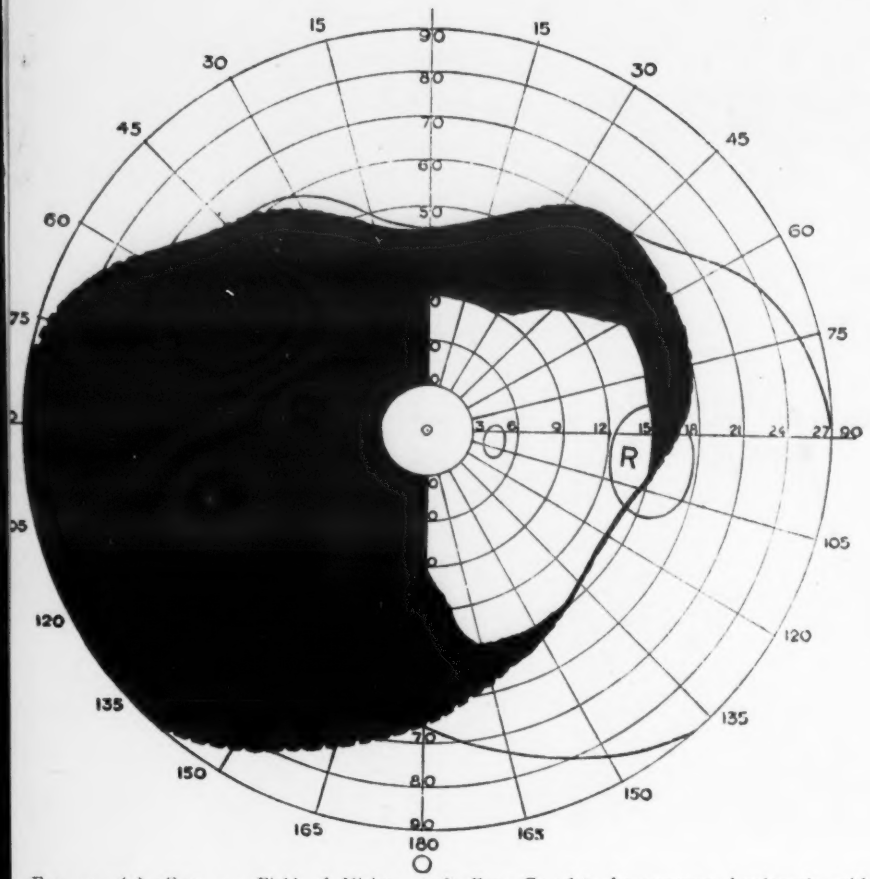


FIG. 12. (a)—Case 14: Field of Vision. Left Eye: Complete homonymous hemianopia with T. D. macular sparing.

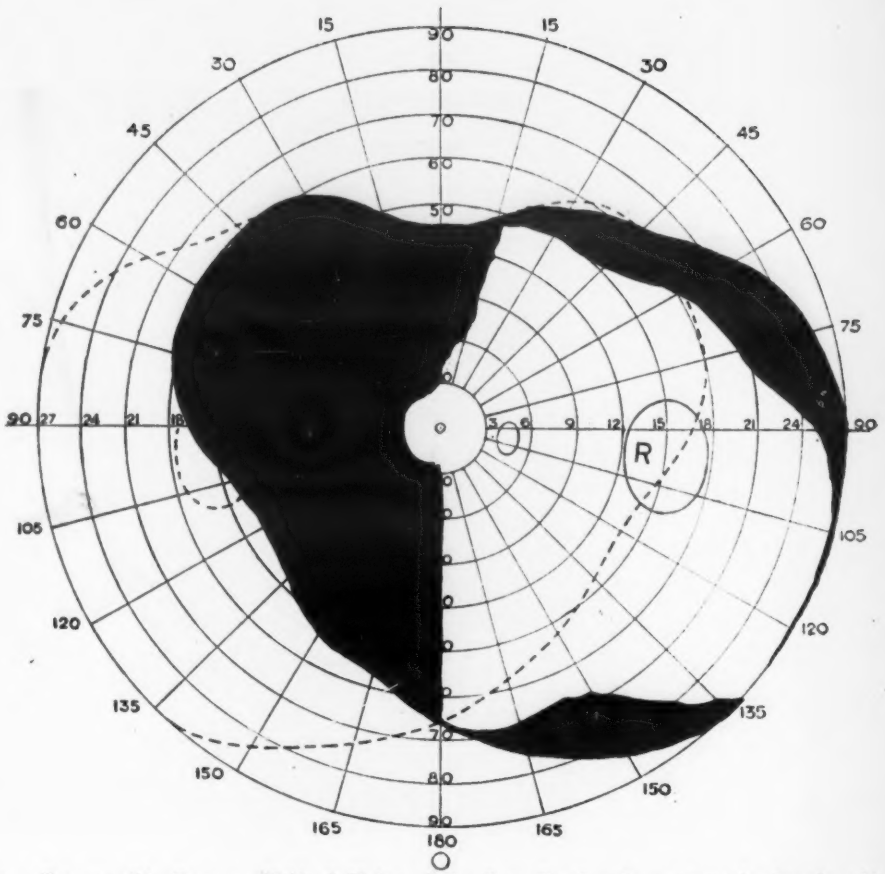


FIG. 12. (b)—Case 14: Field of Vision. Right Eye: Complete homonymous hemianopia with P. T. D. macular sparing.

function, both transient and permanent, associated with these groups of wounds, on account of the longer path taken by the missile, and the greater chances it had of causing cerebral damage, whether it passed in a transverse, sagittal or oblique plane. Many of them were fatal, or death took place in the forward areas before they could reach a Special Center. The prolonged period of initial unconsciousness and the added risk of the missile introducing virulent organisms from the accessory sinuses, or elsewhere, deeply into brain tissue or even the ventricular system, increased the hazards of their nursing and treatment, and made their prognosis worse. In general, the same methods of treatment, in the way of wound toilet, removal of indriven débris and bone fragments (especially from the orbital roof or frontal sinus), control of hemorrhage, and the use of sulphonamides are all applicable, but special attention should be directed towards gentle lavage of the track of the missile, followed by the injection of a sulphonamide cream, the provision of soft rubber drainage for a short period, and the prevention of reinfection, aerocele and fistula formation, from the involved sinus or orbit, by a careful repair or replacement of the torn dura mater as soon as practicable. A few cases of these groups were encountered in the present series, each with its own problems, but it is yet too early to assess their final results, and it is felt that consideration of them should be deferred.

DISCUSSION AND CONCLUSIONS

Most of the lessons to be learned from treating this series of cases have been discussed and pointed out as they occurred. They may be reiterated as follows:

1. The thoroughness of the initial examination and toilet of the wound is more important than the time factor, at least up to four days, as long as prophylactic sulphonamide therapy is maintained during the period of waiting.

2. Surgeons, with field surgical units, must have a knowledge of neurosurgical technic, and be provided with adequate facilities, if this class of wound is to be correctly dealt with in forward areas.

3. Under conditions existing in Middle East, it is better to stabilize these facilities at a place where the patients can be "held" after operation, and so arrangements should be made to transport the patient back as rapidly as possible, preferably by air ambulance, to a Special Center.

4. An alternative plan is the provision of a field surgical unit with operating theater and beds, entirely on wheels, which could keep pace with the advancing or retreating troops or be replaced by another similar unit, when its accommodation was filled.

5. The removal of indriven bone fragments and inorganic débris is more important than the extraction of metallic foreign bodies.

6. Even minute missiles, making a small wound in the scalp and outer table of the skull, are likely to drive large comminuated pieces, of the inner

table, deeply into the brain and cause more extensive damage than the size of the missile and the condition of the patient would indicate.

7. Closure of the tear in the dura mater should be attempted in order to prevent the formation of hernia cerebri, cerebrospinal fluid fistula, and aerocele.

8. Signs of unilateral local and focal damage to the brain do not call for extensive operations, in the absence of signs of compression, but they should be recorded from time to time by observers trained in neurology.

9. The actual concentration of sulphonamide in the cerebrospinal fluid of every patient varies with the same dosage, and must be checked at frequent intervals by colorimetric methods to make sure an adequate concentration is being attained, and maintained, in case of intracranial infection.

10. The advent of the sulphonamide group of drugs, especially sulphadiazine, has altered the outlook for wounds of the head entirely, and none should ever be despaired of, however badly infected and however serious the complications; nor can the final result be predicted.

From a prophylactic point of view, it is felt that something further could be accomplished in the prevention of wounds of the head and subsequent infections by:

(1) The provision of a more modern design of steel helmet, which would fit closer and lower down over the frontal, temporal, mastoid and occipital regions, and which would hinder the entry of rising foreign bodies from explosives which burst on the ground. The present design of steel helmet supplied to the British forces was designed, originally, to afford protection against bullets and the shrapnel of air-bursting explosives; now, not nearly so commonly encountered as splinters from bombs, high explosive shells and land mines. Major P. B. Ascroft, R.A.M.C. (verbal communication) has some very illustrative figures and charts, compiled from his series of some 700 cases, encountered during several Middle East campaigns, to prove these contentions. Their publication and his suggested design for a new helmet are awaited with interest.

(2) The issue of a general order that all troops should have the hair of the scalps closely clipped before going into battle. This would enable them to keep their scalps cleaner and greatly facilitate the work of the Medical Services in the recognition of wounds and their preparation for operation. It would also prevent long hairs and débris from being carried in by the missile. A somewhat analogous procedure exists in the Royal Navy, where personnel are advised either to discard all clothing when going into action, or put on brand new or clean clothes, to lessen the risk of sepsis from old dirty clothing being driven into their wounds.

(3) Every soldier should be given, to keep with his field dressing, a large standard dose of sulphapyradine or sulphadiazine, say four or six Gm., with instructions to take it himself, if able, or have it given to him by a stretcher

bearer, as soon as possible after being wounded. This would be an effective prophylactic for the next 12 hours.

SUMMARY

1. The surgical management of a series of battle casualties of the head, met with in the Middle East, is described and illustrated by numerous case reports.

2. Attention is drawn to certain anatomic and physiologic peculiarities of structures involved, as well as the effects of modern missiles used in Desert Warfare on these structures.

3. A classification of these wounds and the terminology applied to them in the British Army are submitted.

4. The necessity of providing adequate neurosurgical facilities, both in personnel and equipment, for dealing with these cases is pointed out and a general scheme outlined.

5. The lessons to be learned from the cases are discussed, and some prophylactic measures are suggested for future campaigns.

The thanks of the authors are gratefully extended to the undermentioned persons, without whose assistance the treatment of this series of cases and the preparation of this paper would not have been possible.

1. The Director of Medical Services, G. H. Q. Middle East, and the Consultant Neurologist, who authorized the establishment of the Unit as the No. 2 Head Center in the Middle East and made available certain special equipment and drugs.

2. The officers in charge of surgical divisions and surgical specialists of the other general hospitals who referred their cases for opinion and treatment.

3. The anesthetist, the ophthalmic and otorhinolaryngeal surgeons, the pathologist and the radiologists to the Hospital, and their staffs, who readily made their services available at all times.

4. Professor Howard Naffziger, M. D., of the University of California Medical School, and the British War Relief Society of Northern California, U. S. A., who donated special neurosurgical equipment to replace that previously lost by enemy action.

5. Pvt. L. R. Withers, of the Hospital Staff, for the reproductions of the roentgenograms.

6. The Director General of Medical Services, Allied Land Forces, Australia; and the Deputy Director of Medical Services, Australian Imperial Force, Middle East, for permitting the publication of this article.

COMMUNICATIONS BETWEEN THE CORONARY ARTERIES PRODUCED BY THE APPLICATION OF INFLAMMATORY AGENTS TO THE SURFACE OF THE HEART*

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COMMUNICATIONS between the three major coronary arteries can be produced by surgical methods. It was shown experimentally by Stanton, Schildt and Beck[1] that trauma applied to the surface of the heart brought about the development of communications between one coronary artery and another. The type of trauma that was used in this demonstration was produced by abrasion of the surface of the heart. The epicardium was roughened and torn by means of special burs made for this purpose. We are now reporting upon the effect of various inflammatory agents applied to the surface of the heart. We are attempting to find a substance which, when applied to the heart, opens up or develops vascular channels between one coronary artery and another and at the same time does not produce harmful side-effects. A number of inflammatory agents have been used on the heart. Powdered beef bone was used by Beck;[2] aleuronat was used by O'Shaughnessy;[3] talc was used by Thompson;[4] and a mixture of aleuronat, starch, glycerin, commercial gelatin, water and lionite was used by Heinbecker and Barton.[5] A study of this subject is obviously important. Our experiments may be regarded as an introductory study of this subject.

METHOD.—Dogs were used. The material for study was introduced into the pericardial cavity either by making a small opening in the parietal pericardium or by an aspirating needle. The opening in the parietal pericardium was closed tightly by sutures. Three or more experiments were carried out with each substance that was selected for study. The pericardium was opened at the end of one, two and three weeks, under surgical conditions, and the reaction observed. Additional experiments were carried out with those substances that produced a favorable reaction.

Intercoronary communications were determined by a method worked out in our laboratory. We used a mixture consisting of barium sulfate 500 Gm., powdered gelatin 150 Gm. and distilled water 850 cc.[6] This mixture was filtered while hot and was injected at a temperature of 45° C. into the circumflex branch of the left coronary artery and into the right coronary artery. The heart was immersed in water at a temperature of 45° C. during the injection. Injection of the arteries was done at a pressure of 200 mm. mercury for three to five minutes. The specimen was chilled to solidify

* Aided by a grant from the John and Mary Markle Foundation.

the injection mass. It was then fixed in a solution of formaldehyde. Roentgenograms were taken with the heart in such a position as to show the descending ramus of the left coronary artery. The degree of filling in the descending ramus of the left coronary artery was considered as an indication of communications between this artery and the two arteries that were injected. It would appear that the degree of filling has some quantitative significance. The injections were graded as absent, slight, intermediate, and good; and these terms are used throughout this paper as a measure of intercoronary arterial communications. Sections of the parietal pericardium and the epicardium were examined microscopically. When it appeared to be desirable, we attempted to measure the protective effect by ligating one of the arteries. This was done by ligation of the descending ramus of the left coronary artery at its origin several weeks after the substance under investigation had been applied to the heart. The mortality rate of these ligations and a study of the specimens gave information on this subject.

SUBSTANCES FOR STUDY.—The most desirable substance appears to be one that produces a well vascularized type of granulation tissue without producing necrosis of the myocardium, severe exudation and cicatrization. Before beginning the study reported here, Beck had carried out experiments on various substances which he never fully reported. The substances investigated were powdered beef bone, surgical solution of chlorinated soda, kaolin, iron filings, tincture of iodine, ether, alcohol, saturated solution of sodium chloride, solution of glucose, horse serum, acids and alkalies. Of these, powdered beef bone produced the most favorable reaction and was used by Beck in human patients operated upon for coronary artery sclerosis. Chlorinated soda produced compression scars.[7] Kaolin (hydrated aluminum silicate) was absorbed, leaving no reaction, and was found in mediastinal lymph nodes. Iron filings, tincture of iodine, ether, acids and alkalies produced hemorrhagic exudate and severe necrosis. The other substances produced little or no inflammatory reaction.

The only way to determine the effect of any substance is to try it. There was little information to aid us in the selection of materials for study. For this reason we are recording the effect of every substance we studied.

EXPERIMENTAL INVESTIGATIONS

Croton Oil.—Croton oil was mixed with olive oil in the proportion of 1 to 10. Three cubic centimeters of this mixture produced death within five hours. Minute hemorrhages were present beneath the epicardium. There was no fluid in the pericardial cavity. Five cubic centimeters of a 4 per cent mixture produced death within 24 hours. Two cubic centimeters of a 1 per cent mixture produced death in 48 hours. A large quantity of bloody fluid was found within the pericardial cavity in each of these experiments. Capillary hemorrhages were present beneath the epicardium.

Croton oil was mixed with sesame oil in the proportion of 1 to 1000. Five cubic centimeters of this mixture was used in one experiment and one cubic centimeter was used in two experiments. These animals died in three days, two days, and seven days. One had acute cardiac compression produced by 200 cc. of bloody fluid in the pericardial cavity. The thoracic and abdominal cavities contained straw-colored fluid.

The liver showed focal necrosis. The mediastinal tissues in these experiments showed hyperemia. Fibrin was deposited upon the epicardium within a few days. Microscopically, a deposition of fibrin was found on the epicardium and parietal pericardium and these structures showed acute inflammation.

Croton oil, even in high dilution, is a strong irritant and should not be used for this purpose.

Santal Oil.—Santal oil was used in three experiments. Three cubic centimeters produced death within five days in each experiment. A large quantity of turbid fluid was found in the pericardial cavity. A severe inflammatory reaction was present beneath the epicardium and also in the parietal pericardium. Microscopically, there was evidence of acute inflammation in the epicardium with necrosis of the adjacent myocardium. There was an infiltration of polymorphonuclear leukocytes and large round cells in these structures.

Santal oil is a strong irritant when injected into the pericardial cavity and should not be used for this purpose.

Formaldehyde.—Formaldehyde was used in six experiments. Two cubic centimeters of 10 per cent solution was used. In three experiments death occurred within seven days. Fluid was found in the pleural and pericardial cavities. In one experiment death occurred two months later from chronic cardiac compression. The parietal pericardium and epicardium were sealed together and compression developed from the contracture of this scar. In two experiments the descending ramus of the left coronary artery was ligated at its origin ten days after the introduction of the formaldehyde. Death occurred almost immediately after ligation of this artery in each experiment. The coronary arteries were injected and in one of these specimens there were some intercoronary communications present and in the other specimen there was no evidence of intercoronary communications.

Formaldehyde is a strong irritant. It produces exudate and compression scars. It may exert some slight effect upon the production of intercoronary communications but the reaction is too severe for our purpose.

Neutral Acriflavine.—Neutral acriflavine was used in a 30 per cent solution. Two cubic centimeters were introduced into the pericardial cavity in three experiments. One animal died four days later, one died six days later, and one was killed seven days later. Serosanguineous fluid was found in the pericardial and pleural cavities in each of these animals. The parietal pericardium was thickened and a few fibrinous adhesions to the heart were present. Subepicardial inflammation and degeneration of adjacent myocardium were found. Many small blood vessels were present in the pericardium.

Acriflavine is a strong irritant and should not be used for our purpose.

Typhoid Vaccine.—Typhoid vaccine (one billion organisms per cubic centimeter) in doses of two cubic centimeters was introduced into the pericardial cavity in three experiments. These animals were killed at the end of one, two and three weeks. The epicardium and parietal pericardium appeared to be normal in each experiment.

Typhoid vaccine produced no recognizable reaction in these experiments. We should like to suggest that biologic reactions, such as the Schwartzman reaction, should be investigated in reference to this problem.

Sodium Morrhuate.—Sodium morrhuate (Parke, Davis, 5 per cent) was injected into the pericardial cavity in three animals in doses of three cubic centimeters. At the end of one week the parietal pericardium showed a severe hemorrhagic inflammatory reaction consisting of red corpuscles, fibrin, edema and polymorphonuclear leukocytes. There was also an increase in the size and number of blood vessels. Fibrinous adhesions to the epicardium were everywhere present. These did not bleed when broken during operation. The epicardium was thickened and showed a similar reaction. There was little or no fluid between pericardium and heart. At the end of 19 days the inflammatory reaction had almost entirely disappeared. There were no adhesions and epicardium and parietal pericardium appeared to be normal. Microscopically, the parietal pericardium showed resolution of the inflammation with some residual fibrosis. There was no increase in vascularity. At the end of four months the epicardium and parietal pericardium appeared grossly normal and, microscopically, showed some slight fibrosis.

The right coronary artery and the circumflex ramus of the left coronary artery were injected with barium sulfate-gelatin mixture in two specimens that had received sodium morrhuate four months previously. In each of these, the descending ramus of the left coronary artery showed slight injection. The amount of barium present was within the limits found in normal hearts injected in the same way.

Sodium morrhuate produces an inflammatory reaction together with an increase in vascularity during the early stages. These changes are of a temporary nature and disappear after a few weeks. For our purpose it is desirable to select a substance that exerts an effect on vascularity for a long period of time.

Sodium Ricinoleate.—Sodium ricinoleate ("Soricin," Merrill Co., 5 per cent) was injected in quantities of three cubic centimeters in each of three animals. At the end of one week the epicardium and parietal pericardium showed severe inflammatory reaction. Microscopically, a marked extravasation of red blood cells was found beneath the epicardium and also in the parietal pericardium. In one animal that was operated upon for purposes of examination, ten cubic centimeters of serosanguineous fluid was found in the pericardial cavity. Death occurred five days later, and large quantities of serosanguineous fluid were found in the pleural and pericardial cavities. The heart was examined for intercoronary communications and no barium went across to the noncannulated artery. In another experiment the heart was examined at the end of 12 days. At that time, there was no exudate on the heart or on the parietal pericardium. The inflammatory reaction seemed to have subsided markedly. In another experiment the parietal pericardium was opened at the end of 24 days. The inflammatory reaction had almost completely subsided. The parietal pericardium was slightly thickened. There were no adhesions and there was no fluid in the pericardial cavity. The animal was killed at the end of four months. The heart and pericardium appeared normal. The coronary arteries were injected and good intercoronary communications were demonstrated.

Sodium ricinoleate produces a reaction similar to that of sodium morrhuate. A severe inflammatory reaction is produced early. Later the inflammation subsides. There is an early increase in vascularity but it seems to subside as the inflammation subsides.

Iodized and Chlorinated Oil.—Iodized and chlorinated oil ("Iodochoral," Searle) was injected in three experiments in quantities of four cubic centimeters. One animal died at the end of seven days. Large quantities of fluid were found in the pleural and pericardial cavities. A severe cellular reaction was present in the pericardium. There

was no evidence of intercoronary communications in the injected specimen. In another experiment the pericardium was opened at the end of 19 days. A few fine adhesions were found. The inflammatory reaction was mild and almost absent. The oil was saponified and appeared as placques in the epicardium. At the end of three months the reaction had subsided and little or no fibrosis of the pericardium was present. The coronary arteries were injected in this and also in the third specimen at the end of three months and good intercoronary communications were present in each specimen.

This substance produces an early, marked inflammatory reaction which has a tendency to subside after a few weeks. It seems to favor the development of intercoronary communications but the effect is too severe to be used in patients.

Tragacanth.—Tragacanth in doses of two Gm. was used in three experiments. Cardiac compression developed in two experiments. One animal died in two days; the other died in 15 days. The latter was explored by operation the day before death. At operation, fluid was found in the pericardial and pleural cavities. The fluid was removed. The parietal pericardium was thickened and densely adherent to the heart. The adhesions did not bleed when broken. Fluid rapidly reformed in the pericardial and pleural cavities and produced death the following day. The third animal continued to live and was killed at the end of three months. The parietal pericardium was thickened and was adherent to the heart. The inflammatory reaction had subsided. Fibrosis and some blood vessels were found in the pericardium. The three hearts were injected with barium. The animal that died in two days did not show any of the barium in the descending ramus of the left coronary artery. The other two specimens showed a moderate amount of the barium in this artery.

Tragacanth produces a severe exudative reaction and should not be used.

Talc.—Magnesium silicate, Gm. 3, was introduced into the pericardial cavity in three experiments. An inflammatory reaction developed in a few days in the parietal pericardium and epicardium of these animals. These tissues had a gelatinous exudate and were joined by fibrinous adhesions which were easily broken and from which there was no bleeding. Later, the talc collected in localized areas which became walled-off. Elsewhere the reaction was mild and the epicardium and parietal pericardium resembled the normal. At the end of three months thick avascular scar tissue was found in the pericardium. In one experiment scar tissue produced signs of cardiac compression. In a series of ten additional experiments, three Gm. of talc was introduced into the pericardial cavity and the animals were allowed to recover. Two weeks after the talc was introduced, these animals were reoperated upon and the descending ramus of the left coronary artery was ligated at its origin. Three of the animals recovered from this ligation and seven died.

On the basis of these experiments, it appears that talc did not exercise a beneficial effect when this artery was ligated. These results were similar to those obtained following ligation of the descending ramus of the left coronary artery in control experiments. They do not agree with the beneficial results reported by Thompson.[4]

Silicon.—Two Gm. of powdered silicon (Merck) was introduced into the pericardial cavity of three animals. The early reaction consisted of inflammation and adhesions. Later on, these adhesions did not seem to be well vascularized, and there was no bleeding when the adhesions were broken. There was some thickening of the peri-

cardium. All of the animals lived and were killed at the end of three months. In two animals the coronary arteries were injected with barium as usual. There was no evidence of intercoronary communications in these specimens.

The reaction produced by silicon is not favorable.

Sand.—Sand (Merck), ten Gm. was used in each of three experiments. At the end of seven days adhesions were present between the parietal pericardium and epicardium. These were easily broken without bleeding. The surface of the heart was reddened and injected. At the end of 21 days the inflammatory reaction was mild. The sand had collected posteriorly at the base of the heart. At the end of three months' time a few adhesions were present. The inflammatory reaction had subsided. The parietal pericardium was thickened. The coronary arteries of two specimens were injected in the usual way at the end of three months. One specimen showed good filling of the descending ramus of the left coronary artery and the other specimen did not show any barium in this artery.

The reaction produced by sand is not favorable.

Water Glass.—Water glass, which is a solution of sodium silicate, was placed in the pericardial cavity in five animals. The amount used varied from one to five cubic centimeters. Death occurred in each experiment within two weeks. The tissues that came into contact with the water glass appeared brown, as though they had been burned. There was much exudate in the pleural and pericardial cavities.

Water glass is a strong agent causing exudation and necrosis.

Agar.—Agar in powdered form, in doses of three Gm., was used in four experiments. Death occurred in each experiment 1, 3, 10 and 11 days later from cardiac compression. The pericardial cavity was filled with thick serosanguineous fluid. Slight hyperemia of the parietal pericardium and epicardium was found. Some fibrinous adhesions were present. The reaction in the pericardium and epicardium varied from a mild to a moderately severe inflammation. Fluid was found in the pleural cavities and also in the abdomen. The right coronary artery and the circumflex ramus of the left coronary artery were injected. Moderate injection of the descending ramus of the left coronary artery was found in one specimen and no injection was found in the other three specimens.

The effect of agar is not favorable.

Cotton.—Cotton gauze was used in four experiments. One layer of surgical gauze was placed between heart and pericardium. An inflammatory reaction was found early, with adhesions which were well vascularized. Later, these adhesions became dense and the inflammation subsided. The vascularity was less at the end of three months but blood vessels were found in the adjacent scar. There was no formation of fluid in the pericardial cavity. The coronary arteries were injected in three specimens at the end of three to four weeks, and one specimen showed a slight amount of barium present in the descending ramus of the left coronary artery, and two specimens showed no injection of barium in this artery.

A paste consisting of 0.4 Gm. of finely cut cotton and two Gm. of starch was introduced into the pericardial cavity in five animals. Subsequent examination showed adhesions between the parietal pericardium and the heart. The adhesions were dense in those locations where cotton had collected between heart and pericardium. Elsewhere the adhesions were easily broken. The parietal pericardium showed slightly increased vascularity. The descending ramus of the left coronary artery was ligated and one animal survived and two died. The coronary arteries were injected with barium and

the intercoronary communications were good in two specimens, slight in one specimen and absent in two specimens.

Cotton produces a relatively mild inflammatory reaction early with the formation of blood vessels but later the vascularity becomes less marked. Cotton is not particularly effective in increasing the vascularity in these structures.

Aleuronat.—Aleuronat was introduced into the pericardial cavity in four experiments. Three Gm. was used in each. One of these was examined at the end of eight days. The parietal pericardium bled freely when it was incised. It was greatly thickened and showed fibroblasts and cellular infiltration. A large quantity of bloody fluid was present in the pericardial cavity. It clotted upon standing. There was a deposit of fibrin upon the epicardium and many adhesions were present. This animal died at the end of 17 days from acute cardiac compression due to fluid in the pericardial cavity. The pleural cavity also contained fluid. The other three animals developed compression of the heart and died in 10, 24 and 30 days, respectively. In each of these, thick serosanguineous fluid was present in the pericardial and pleural cavities and clear straw-colored fluid in the abdomen. The parietal pericardium and epicardium were thickened and were avascular. There was a marked deposition of fibrin on the heart and there were many avascular adhesions to the heart. The coronary arteries were injected with barium in these specimens and in none of them was there any evidence of intercoronary communications.

Aleuronat produces a severe, exudative, inflammatory reaction. There was an early increase in vascularity in the parietal pericardium of one animal but in three hearts in which the coronary arteries were injected intercoronary communications were not found.

Lionite, Aleuronat and Starch.—(Heinbecker and Barton)[5]: A mixture of lionite, aleuronat and starch was made in the proportions used by Hernbecker and Barton. Eight to ten Gm. of this mixture was placed in the pericardial cavity in ten animals. One cubic centimeter of sodium morrhuate was applied to the surface of the heart before this mixture was introduced. These animals survived this procedure, and two months later the descending ramus of the left coronary artery was ligated at its origin. Four of these survived and six died. This mortality rate is similar to that obtained in control experiments. The deaths occurred within 24 hours after ligation. Early death after ligation of this artery occurred in normal hearts and in those specimens in which the preparation had provided little protection to the heart. The arteries in these six specimens were injected with barium and they showed intercoronary communications to be of intermediate grade in two, slight in two, and absent in two. The four animals in which recovery took place after the artery was ligated were killed several months later. Good intercoronary intercommunications were found in each specimen. Arterial ligation is an effective stimulus in producing these communications. The infarct in these specimens was large in three and intermediate in size in one. It is to be noted that the size of the infarcts also indicated that the protection afforded to the heart was not great. In other words, the blood-bath to the ischemic myocardium was not sufficient to prevent the usual necrosis and replacement of scar tissue. Cardiac compression developed in one of these experiments after the artery was ligated. The compression scar was removed and the condition was cured.

Nine additional experiments were undertaken using the Heinbecker-Barton mixture. One cubic centimeter of sodium morrhuate was applied to the surface of the heart and eight to ten grams of the lionite-aleuronat-starch mixture was introduced. Four of these

animals died of cardiac compression in 11 days to six weeks after this material was placed in the pericardial cavity. One died of distemper two weeks later. Four anima's remained alive in this series and three of them developed cardiac compression. The compression scars were removed by operation, and all three recovered. These animals were killed several weeks later. The specimens of the entire group were studied for intercoronary communications. Three specimens showed no evidence of intercoronary communications; two showed slight filling of the descending ramus of the left coronary artery and four showed intermediate filling of the artery. Good communications were not found in any of these specimens.

Microscopic study could not be made because of the lionite. A severe inflammatory reaction with exudation was produced by these inflammatory agents. There was a great tendency for cardiac compression to develop following the use of these substances. The lionite had a tendency to collect in masses posteriorly to the heart.

These substances, according to our studies, are not effective in producing intercoronary communications, and the reaction is severe. Our results are not as favorable as were those obtained by Heinbecker and Barton.

Human Skin.—Three Gm. of dried, sterilized human skin, cut into small pieces, was placed in the pericardial cavity in three experiments. Death occurred in 2, 9 and 10 days. The pericardial cavity contained large quantities of exudate which had the appearance of pus. The epicardium was covered with a deposit of fibrin. The parietal pericardium was several times its normal thickness and, in one specimen, there were numerous blood vessels. The inflammation in the pericardium was severe. The coronary arteries were injected with barium. One specimen showed good filling of the descending ramus of the left coronary artery; one showed slight filling and one showed no filling of this artery.

Skin had a severe exudative reaction and is not satisfactory.

Heinbecker-Barton Mixture, Sodium Morrhuate and Human Skin.—Eleven experiments were made in which eight Gm. of Heinbecker-Barton mixture, 1 cc. sodium morrhuate, and one Gm. human skin were introduced into the pericardial cavity. Death occurred in two of these animals from compression; death occurred in three from distemper; six were killed after four months. The coronary arteries were injected with barium in the specimens' and the communications were graded as absent in four, intermediate in three, and good in three. It appeared that there was an increase in intercoronary channels in these experiments.

We believe it is advisable to determine what single substance produces the most favorable reaction and not to use many different substances at one time.

Asbestos (calcium and magnesium silicate).—Three Gm. of calcium and magnesium silicate, in the form of asbestos, was placed in the pericardial cavity in three experiments. At the end of one week the parietal pericardium was slightly thicker than normal and was well vascularized. Brisk bleeding occurred when it was cut. It was adherent to the heart and the adhesions bled when they were broken. A few cubic centimeters of fluid was present in the pericardial space. The surface of the heart appeared to be hyperemic. Marked cellular infiltration was present at the end of one week. The cellular reaction subsided later, and many arterioles and capillaries were formed at the end of two weeks (Figs. 1 and 2). The epicardium lost its identity and the inflammatory process was in direct continuity with muscle fibers. The mediastinal tissues and fat showed increased vascularity. These tissues bled when cut. When the lung became adherent to the outer surface of the parietal pericardium the surfaces bled

freely when separated. At the end of four months the sections showed an increased number of blood vessels and also some scar tissue. The cellular reaction had generally subsided at that time, and foreign body giant cells were present. The coronary arteries were injected with barium at the end of three to four months. The filling of the descending ramus of the left coronary artery was good in two specimens and was slight in one specimen.

Many additional experiments were carried out with this form of silicate (asbestos). It was found that the amount of asbestos that produced the most favorable reaction was about 0.1 or 0.2 Gm. Large amounts occasionally produced a subepicardial hematoma. In one experiment a walled-off collection of fluid between parietal pericardium and heart produced compression of the heart. Thick dense epicardial scars were pro-

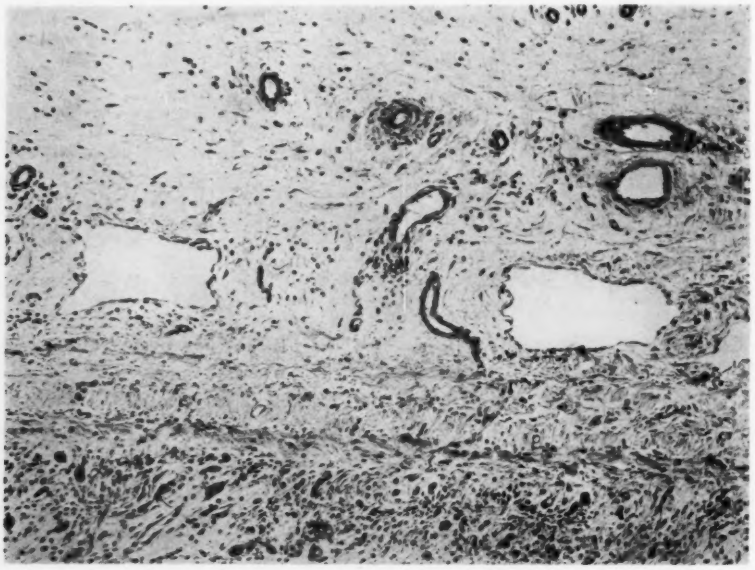

FIG. 1.—Photomicrograph of visceral and parietal pericardium showing foreign body reaction produced by silicate. Blood vessels are shown. (× 94)

duced by large quantities of asbestos. In several experiments fluid was found in the pleural cavities. When the coronary arteries were injected with barium intercoronary communications were present in every specimen.

Nine experiments were carried out in which about 0.5 Gm. of silicate in the form of asbestos was used. These experiments were allowed to proceed for a period of two weeks. At the end of this period operation was carried out and the descending ramus of the left coronary artery was ligated at its origin. Six of these animals survived ligation of this artery; three died. The coronary arteries of these three specimens were injected with barium and good intercoronary communications were found in two of the specimens. The six animals that survived the operation were killed several months later and the size of the infarcts noted. In one of these specimens there was no infarct; in three specimens the infarct was small, and in the remaining two specimens the infarct was classified as intermediate in size. There were no large infarcts.

In our experience, the mortality following ligation of the descending ramus of the left coronary artery at its origin in normal animals was 35 out of 50 experiments, or 70 per cent. In these nine experiments treated with asbestos, six animals survived a second operation at which this artery was ligated, a mortality of 33 per cent. We interpret this as a reduction in mortality. We can also state that the infarct was of

smaller size in the experiments in which asbestos had been used. For a discussion of mortality and size of infarct in 50 normal hearts in which the descending ramus of the left coronary artery was ligated at its origin, the reader is referred to the article by Stanton, Schildt and Beck.[1]

Another series of ten experiments was carried out in which the surface of the heart was rubbed by a bur in such a way that the epicardium was torn and some of it was removed in shreds. In these experiments 50 to 100 milligrams of asbestos was rubbed into the surface of the heart by a bur. These animals survived this procedure. Most of them showed an elevation in temperature of about one degree centigrade for a week or ten days. A compression scar did not develop in any animal. One week later the

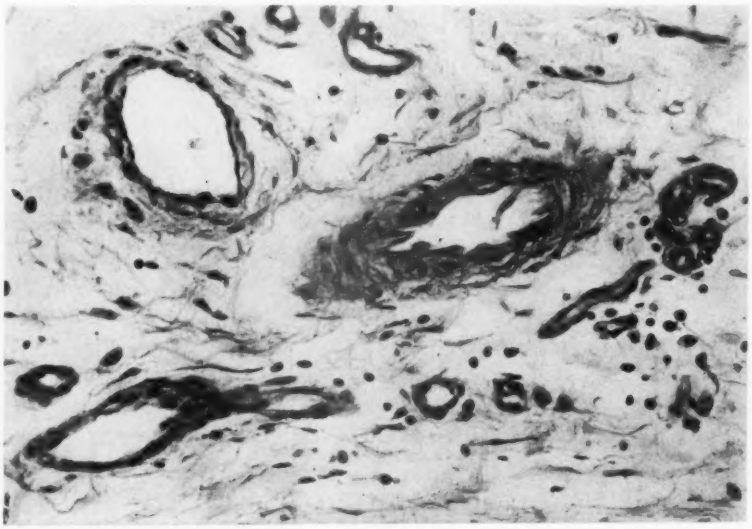

FIG. 2.—Photomicrograph showing arteries and veins produced by silicate on surface of heart. (×297)

animals were operated upon again and the descending ramus of the left coronary artery was ligated at its origin. Seven of these animals survived ligation and three died, a mortality of 30 per cent. One of these died a few minutes after the artery was ligated and the injection specimen showed good intercoronary communications. Two died within 24 hours after ligation of the artery. The seven animals that survived ligation of the artery were killed at the end of six weeks. Two of these showed focal areas of myocardial fibrosis and no gross infarct; two had infarcts of intermediate size, and three had large infarcts. Each of these specimens showed good intercoronary communications. The common arterial bed in these specimens was produced by the inflammatory reaction produced by abrasion and by the asbestos plus the delayed stimulus of the arterial ligation itself.

A paste consisting of 0.2 Gm. of asbestos and a small amount of tragacanth was placed in the pericardial cavity in six animals. One of these died one month later and examination showed fluid in the pleural cavities. Ligation of the descending ramus of the left coronary artery was carried out in four experiments. Two of these animals recovered and two died. Injection of the arteries with barium in these four hearts showed good intercoronary communications in the two specimens where recovery occurred, slight filling in another and no filling in another.

The effect of a paste made of tragacanth and asbestos was not as good as that with the powdered asbestos alone.

DISCUSSION.—On the basis of these experiments it appears that silicate in the form of powdered asbestos produced the most favorable reaction. The inflammatory process brought about by asbestos was well vascularized. Amounts of about 0.2 Gm. distributed over the entire surface of the heart produced a more favorable reaction than did a larger quantity. It is slightly exudative in its effect but this is not severe and it does not preclude its use when employed in small quantities. It does not produce compression of the heart due to the formation of scar tissue. The inflammatory effect persists over a period of several months. We have used it on human patients and the effect was satisfactory. The wound in the chest wall healed nicely in these cases. Measurements of the beneficial effect are indicated by data obtained by ligation of the descending ramus of the left coronary artery at its origin. Mortality in 50 normal animals following ligation of this artery was 68 per cent. Mortality in animals in which asbestos had been applied to the surface of the heart previous to ligation was 32 per cent (six out of 19 animals). The size of the infarcts in the latter group was smaller than in the control group. Indeed, in a few of the specimens treated by asbestos there was no infarct after the descending ramus of the left coronary artery was ligated. In the control group a definite infarct always developed after ligation of the artery. Also intercoronary communications were better developed in the specimens in which asbestos had been used as compared with the intercoronary channels found in normal hearts.

Some of the substances used in the experiments produced death. This was brought about by exudation of fluid or by the development of compression scars. Some of the substances produced little or no reactions; others produced a rather indifferent degree of vascularization; others produced good vascularization early but after several weeks the degree of vascularization became less marked. It seems to be desirable to use one substances rather than a combination of substances. It needs scarcely be stated that one should not be indiscriminate in what substance is placed in the pericardial cavity and also in the amount used.

Heinbecker and Barton carried out experiments in which a mixture of gelatin, aleuronat, starch, glycerin, water and lionite was introduced into the pericardial cavity. In some experiments these authors also used sodium morrhuate. After these substances were introduced the pericardium was closed and then the pericardium was sutured to the restrosternal tissues. Fourteen animals were prepared in this manner. Four to 12 weeks later, these animals were again operated upon and the descending ramus and the circumflex ramus of the left coronary artery were ligated about one centimeter from the aorta. Eight of the 14 animals died and six survived. Infarcts were not found in these specimens.

We carried out experiments in which we tried to repeat this procedure. We were not able to get any animals to survive ligation of both of these arteries in one step. According to our studies the reaction produced by these irritants was not as satisfactory as that produced by powdered asbestos. This mixture of substances produced death in some of our experiments by the

formation of fluid. The tissues, as found in our experiments, were not as richly vascularized as we found after the use of asbestos.

O'Shaughnessy reported favorable results by the use of aleuronat. We found that aleuronat produced a severe exudative reaction, with an early increase in vascularity but, later, no increase in vascularity was found.

Thompson reported favorably on the use of talc. Our experiments failed to confirm his highly beneficial results. It is interesting to note the different reactions produced by various silicates. Talc is a soft, unctuous mineral consisting of magnesium silicate. Asbestos is fibrous magnesium and calcium silicate. Water glass is a solution of sodium silicate. Silicon is the element. Kaolin, which is hydrated silicate, was absorbed and was found in lymph nodes. It produced no local reaction.

CONCLUSIONS

The application of asbestos to the surface of the heart brings about the development of new communications between one coronary artery and another.

It reduces the mortality following ligation of a coronary artery.

It reduces the size of the infarct that develops after a coronary artery has been ligated.

The application of asbestos to the surface of the heart is a safe surgical procedure in animals, provided a dosage of about 0.1 to 0.2 Gm. be used rather than larger doses.

Inflammatory agents used on the heart may not be without harmful side-effects, and they should not be used indiscriminately.

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STAB WOUND OF THE HEART

CASE REPORT OF SUCCESSFUL SUTURE

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THE FREQUENCY OF OCCURRENCE of stab wound of the heart at Harlem Hospital is revealed in the following tabulation of the number of admissions for this condition found in each 12 months of the five-year period from January 1, 1938, to August 1, 1942. There were 28 such cases recorded; five being admitted in 1938; ten in 1939; five in 1940; six in 1941, and two in 1942. Twenty-one of the total number of admissions were operated upon, and nine recovered. Seven died within one hour after admission and seven died during operation. Three of the above nine recoveries have been previously reported, two by one surgeon,[3] and one by another.[2] The remainder were operated upon by four other surgeons.[1]

So many operative successes can be attributed, in part, to the nature and extent of the injury to the heart and to the nature and extent of associated injuries. Other factors in this respect are the immediate recognition of the gravity of the injury and the necessity for early operative intervention. We have come to recognize the fact that extensive and serious damage to underlying structures all too frequently accompany the small surface laceration presenting an innocent appearance. Hence, a policy of exhaustive work-up and close clinical observation has been adopted in each case until the extent of the injury has been determined and the danger of mistaken diagnosis is eliminated.

Factors of importance in operative technic and in postoperative care, which directly influence success or failure, are the chief concern of the surgeon. They include the type of anesthesia; the kind and site of the incision for the approach to the pericardium; the management of the heart and mediastinum during the procedure; the closure of the incision and the indications for drainage; the close attention during the postoperative period to prevention of tension in the pleural cavity from fluid and from air; and the prevention of cardiac compression from fluid allowed to accumulate in the pericardial sac under tension.

The appended case report is that of the last patient in the above series:

Case Report.—A well-nourished white male, age 25, was admitted to Harlem Hospital by ambulance, June 20, 1942, at 12:10 A.M., having been stabbed in the chest during a holdup one hour previously. When first examined the patient was in shock, cold and clammy. Actively flowing dark red blood was issuing from a three-quarter-inch stab wound in the left chest in the sixth interspace at the outer border of the sternum. The patient was conscious, oriented, exceedingly pale, with a blood pressure of 60/40, and a fluttering pulse barely discernible at the wrist. A diagnosis of stab wound of the heart was made and the patient prepared for immediate operation. A

roentgenogram of the chest was taken on the way to the operating room, and an intravenous infusion of glucose 5% in saline 1000 cc. was started. No other medication was given at this time. It is estimated that the operation was started approximately four and one-half hours after the injury.

Operation.—Under ether anesthesia, a vertical incision was made over the left border of the distal two-thirds of the sternum down to the bone. A four-inch incision at right angles to this and extending outward over the fifth rib was then made, and about two inches of the fifth and sixth ribs were removed subperiosteally, together with their cartilages and a small portion of the outer border of the sternum. The pleural cavity was accidentally opened during this procedure. The collapsed and loosely-flapping lung was immediately grasped with a ring clamp, which was then allowed to hang over the edge of the wound. This procedure has been found desirable for combating the immediate effects of open pneumothorax. The pericardium was then opened vertically and several large blood clots were removed from the pericardial sac. Dark red blood spurted from the right ventricle with each systole and rapidly filled the pericardial sac. The bleeding points in the heart were seen to result from a through-and-through laceration of the right ventricle; *i.e.*, through the anterior wall into the chamber and out through the posterior wall; proceeding through the dome of the diaphragm at the base of the pericardial sac and, presumably, into the liver. The lacerations of the anterior and posterior walls measured approximately one centimeter in length. The crazily fluttering heart was grasped in the hand and steadied with a fixation suture of catgut through the apex of the heart. The wound in the anterior wall of the right ventricle was closed with interrupted No. 0 chromic catgut. The wound in the posterior wall of the right ventricle was closed with the same type of suture in a similar manner. Active bleeding from the wound in the diaphragm was controlled with interrupted sutures of No. 2 plain catgut. When the fixation catgut suture was removed from the apex of the heart muscle, blood spurted through the opening with each systole, making it necessary to apply several interrupted catgut sutures of No. 0 chromic through the myocardium to effect complete hemostasis. The pleural cavity was then aspirated of all free blood and blood clots, and a stab wound was made through the seventh interspace in the midaxillary line for the purpose of drainage. A fenestrated one-quarter-inch rubber tube was passed through the stab wound to the costophrenic angle posteriorly, and was fastened in place by a silk suture to the skin, through a rubber cuff. A fixation suture of catgut through the margin of the lung at the interlobar fissure and to the parietal pleura at the line of the incision anchored the latter and aided in stabilizing the mediastinum. The transverse incision was then closed with No. 2 chromic catgut through the parietal pleura, muscle and deep fascia. The pericardial sac was left open to drain into the pleural sac, and was not flushed with saline.[4] The vertical incision was then closed with continuous catgut, so that the pleural cavity was rendered air-tight. Because of the proximity of the stab wound to the incisions, the wound was filled with sulfathiazole and the skin was not sutured. At the end of the operation the condition of the patient seemed good, except for fluid loss. Two hundred cubic centimeters of blood plasma from the blood bank was administered during operation, immediately followed by 800 cc. of physiologic saline. Immediately postoperative the patient was placed in an oxygen tent. Arrangements had been made during this time for cross matching with a professional donor, so that within one hour after operation the patient was receiving a citrated whole blood transfusion.

Postoperative Course.—During the postoperative period the patient was given sufficient sedation, at regular intervals, to overcome restlessness, excitation, and pain, so that he appeared comfortable at all times.[1] The thoracotomy tube was attached to a Cassasa[1] bottle for underwater drainage, and tested at frequent intervals for patency.[1] The thoracotomy tube was removed on the fourth day, and the wound healed completely

two weeks later. Twelve hours after operation a blood transfusion of 500 cc. was administered, and fluid balance maintained by continuous drip infusion of 5% glucose in physiologic saline. Chemotherapy by mouth was not employed; the temperature ranging from 100° to 102° F. until the fourteenth postoperative day, when it receded to 99° F., then fluctuated to 101° F. until the twenty-first day, after which it remained normal. The patient was kept in the oxygen tent for approximately two weeks. Roentgenograms of the chest on the eighth postoperative day showed clouding at the left base. The trachea had shifted to the right. An electrocardiogram, taken 12 days after operation, showed: Auricular rate 95, Ventricular rate 95, L_1–R T elevated, Q present; L_3–R T depressed. P–R interval 0.16 seconds, Q R S interval 0.08 seconds. Elevation of the R T segments denotes early change following pericardial injury.

The left lung filled out rapidly, and respirations became deeper. About three weeks after operation thoracentesis of the left chest posteriorly yielded 55 cc. of serosanguineous fluid. The patient was allowed out of bed 30 days after operation, and was discharged on the thirty-fourth day. When last examined, December 20, 1942, he was apparently quite well.

COMMENT.—A choice of incision for transthoracic approach to the pericardium and heart is based upon: (1) The rapidity and ease of adequate exposure for rib resection and exposure of the pericardium and heart. (2) The rapidity and effectiveness of air-tight closure. For this purpose a vertical incision downward at the lateral border of the sternum, then curved outward over the fifth rib, permits easy access for removal of the fourth and fifth ribs, as well as the formation of a skin flap that permits air-tight closure at the end of the operation.[4] The T-shaped incision employed in this instance necessitates the raising of two flaps outward to expose the ribs but permits a greater exposure of the pericardium and heart with better visualization of the base of the pericardium and dome of the diaphragm beneath. Its cosmetic after-appearance compares less favorably.

This experience of passing a suture through the apex of the heart for stabilization demonstrates such a procedure to be unnecessary and harmful. The edges of the laceration in the myocardium can be brought together effectively to accomplish suitable closure if they are approximated with Allis' clamps, provided the latter are held gently and without traction. Such a procedure will avoid the necessity of closing the puncture wound made by a fixation suture through the myocardium. The edges of the incised pericardium were not sutured. Bleeding from these edges appeared insufficient to warrant the added procedure of suturing for control of possible hemorrhage after the blood pressure has risen. Complete and thorough removal of all blood clots and free fluid blood from both the pericardial and pleural sacs by suction is essential to lowered morbidity. The pericardial sac must be left open for drainage into the pleural sac so that collection of pericardial fluid, to the point of incurring danger of cardiac compression, with its fatal sequence, will be prevented.[4] The amount of drainage from the pleural cavity for the first few days postoperatively is sufficient to warrant the routine use of the thoracotomy tube through a separate stab wound in the axilla. Aspiration of accumulated fluid and control of tension pneumothorax requires careful

attention to their occurrence, so that immediate relief can be obtained by thoracentesis.

It appears essential, postoperatively, to maintain as complete relaxation and comfort of the patient as possible and to provide sufficient free oxygen to offset the loss sustained by reason of the collapsed left lung.[1] The need for oxygen administration decreases as the collapsed lung expands and sufficient time has elapsed for the myocardium to heal. Stabilization of the mediastinum in the presence of sudden pneumothorax is easily accomplished by grasping the lung margin with a ring clamp.[4] This is then allowed to hang over the edge of the wound while the operation is in progress and, when completed, the two lobes of the lung are fixed to each other and then to the parietal pleura by suture.

Fluid loss must be overcome by immediate administration of plasma, whole blood transfusion or physiologic saline administrated parenterally, as soon as the bleeding points are controlled.

Fine chromic catgut for suturing the myocardium appears to be as effective as silk and obviates the introduction of nonabsorbable material.

Allowing the skin edges to remain open and suffusing the tissues with sulfonamide compounds appears unnecessary. Experience with immediate closure has demonstrated that the wound heals *per primam*.

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THE SURGICAL MANAGEMENT OF SOLITARY CYSTS, OR CYST-LIKE STRUCTURES, OF PULMONARY ORIGIN

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The terminology dealing with cyst-like structures of the lung is very much confused and the etiology of this condition, particularly as to whether congenital or acquired, has been under considerable controversy. It is our purpose to present six cases that have come under our observation because of certain accidents which occurred due to the presence of a cyst-like structure in the lung, or derived from lung tissue, and to discuss the surgical measures which were employed in dealing with these complications. In some instances the congenital nature of the cyst was obvious, in others it was open to question, and here the controversial nature of the lesion is discussed. One additional case is mentioned where a pulmonary cyst was present which has never given rise to symptoms.

The first account of a case of pulmonary cystic disease in the American literature was an autopsy study made by Koontz,[1] in 1925. This author collected 108 cases from other countries. The next year, Miller[2] reported the clinical course of an infant who died of a ruptured pulmonary cyst. Since this time there have been many papers dealing with all aspects of this abnormality; the most complete account of the whole subject being the monograph of Sellors,[3] published in 1938, based on a study of 32 cases. This author collected over 400 cases in the literature including both solitary and multiple varieties. He points out that this figure is an entirely inadequate expression of the incidence of the disease and that, though uncommon, pulmonary cysts are certainly not a "medical curiosity."

Solitary cysts of pulmonary origin usually present themselves for treatment because of some accident to the cyst, such as infection or alteration of the mechanical air-exchange through a connecting bronchus. Both of these accidents may be further complicated by rupture. Quite frequently the fact that a cyst, or cyst-like structure, underlies the pulmonary disease is not at first recognized due to the fact that empyema, tension pneumothorax, or a combination of the two masks its presence. Not infrequently a mistaken diagnosis of lung abscess is made when a solitary cyst becomes infected. In these cases, as pointed out by Sellors,[4] the final differentiation rests with the pathologist. Once the underlying condition has been made clear, removal of the cyst, the cyst-bearing lobe, or an entire lung may be required properly to deal with the condition. Before this can be accomplished, however, it may be necessary to treat an empyema or "lung abscess" until the infection has been cleared up.

All of the six cases to be reported came for treatment because of some

accident to the cyst. It is interesting to note that in only three of the cases was a positive diagnosis of cyst made when the case was first seen. There were nearly as many types of complications as there were cases. These complications were: Infection of the cyst without rupture; infection of the cyst with rupture and the formation of pyopneumothorax; progressive expansion of the cyst after the subsidence of infection; rupture of the cyst without infection but with the presence of a ball-valve and the formation of a tension pneumothorax; and rupture of the cyst with the discharge of sterile fluid into the pleural cavity.

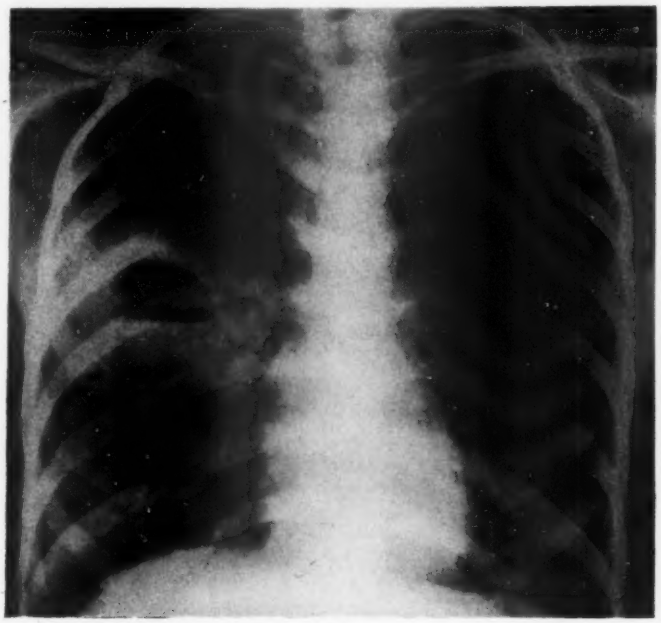

FIG. 1.—Case 1: Appearance of chest on admission. The cystic cavity contains fluid and residual lipiodol.

CASE REPORTS

Case 1.—The first case* is that of a female, age 18, who was admitted to the Mary Hitchcock Memorial Hospital in January, 1937, with a history of having had several attacks of pneumonia in infancy, each one leaving her with increased cough, so that since the last attack of pneumonia, at the age of 12, she had raised from 100 to 150 cc. a day of yellow, foul sputum. There was also occasional hemoptysis. Shortly before admission, a routine roentgenogram taken at the patient's school revealed a lesion of the right lung. She was then sent to a neighboring tuberculosis sanatorium where lipiodol bronchograms were taken. Following this the patient became acutely ill with increased cough, fever and sweating. She lost considerable weight and for some days before admission had been unable to lie flat in bed because of aggravation of her cough in this position.

A roentgenogram of the chest taken on admission is shown in Figure 1. This demonstrates that the cystic cavity is half filled with fluid and in the bottom there is

* Previously reported in the New England Jour. of Med., **222**, 579–584, 1940.

a small amount of residual lipiodol. After nine days of postural drainage, roentgenograms showed complete emptying of the cystic cavity (Fig. 2).

In view of the large size of the cyst and the long duration of the history, it was thought likely that it was of congenital origin and was probably lined with epithelium. Therefore, drainage, either by open thoracotomy or catheter, was thought out of the question, and either enucleation of the cyst or lobectomy was considered the treatment of choice. Therefore, on February 16, 1937, exploratory thoracotomy was performed; and it was found that the cyst was so deeply embedded in the upper lobe that it was necessary to remove the lobe in order to get rid of the cyst. Due to dense adhesions

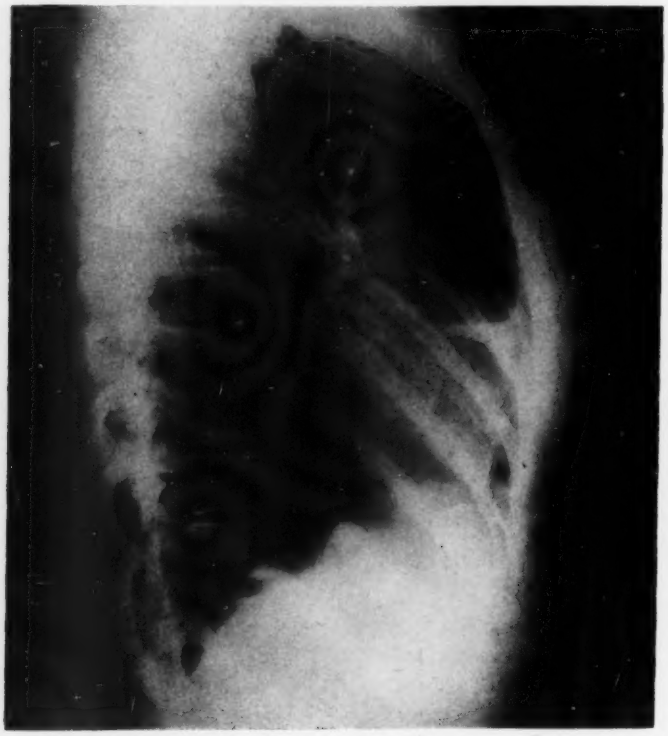

FIG. 2.—Case 1: Lateral view after a short term of postural drainage.

in the lower part of the chest the presence or absence of a middle lobe was not proven, though it was observed that the cyst had a single bronchial communication arising from the upper lobe bronchus as a separate branch. The cyst was opened during the process of removal and, in spite of this, the chest was closed without drainage.

Following operation the patient developed a pure hemolytic streptococcic empyema, and, on February 23, 1937, treatment was begun with "red prontosil," given intramuscularly and directly into the empyema cavity. In five days the cultures were sterile from the pleural cavity and medication was discontinued. The temperature immediately returned to normal after discontinuance of the prontosil, and the patient made an uneventful recovery. The gross specimen is shown in Figure 3.

On examination, the cyst contained all the structures of a bronchus, since its lining consisted of flattened bronchial epithelium and the wall itself contained cartilage. The lung tissue surrounding the cyst showed no changes except for an increase in interstitial tissue in some areas.

The lower lobes failed to overexpand sufficiently to occupy the space left by removal of the upper lobe, and one year later the patient entered the hospital with a return of empyema in this space. This time there was a mixture of organisms and there was subcutaneous emphysema under the tissues of the back due to a bronchial fistula. The cavity was drained through the old incision, resulting in prompt recovery from the empyema; and then a posterior thoracoplasty, removing segments of the first five ribs, was performed in one stage. This resulted in complete recovery. The patient has no cough or sputum, has since been married and has been delivered of a healthy baby without ill effects.

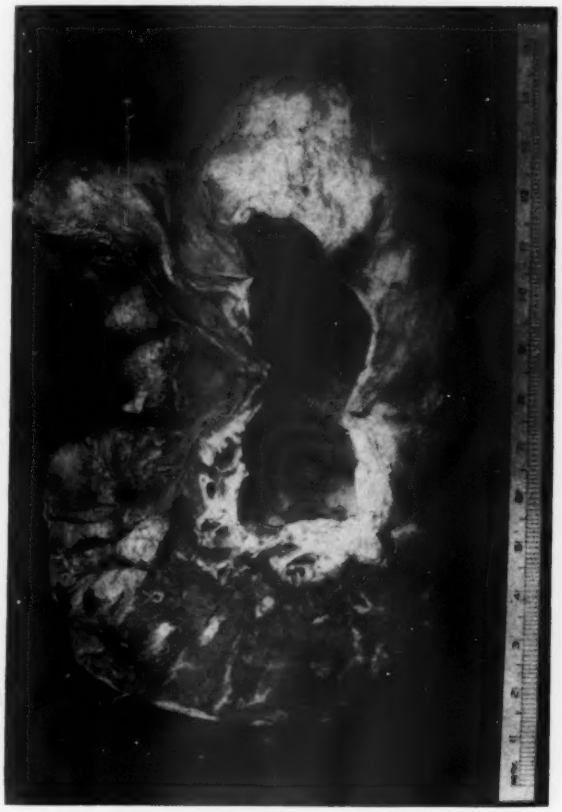

FIG. 3.—Case 1: Specimen removed at operation consisting of the right upper lobe and cyst.

SUMMARY: A six-year follow-up has been obtained on this case following right upper lobectomy for an infected cyst, the congenital nature of which can hardly be questioned. There was failure of the other lobes to overexpand and fill the upper lobe space; and, one year after lobectomy, a bronchopleural fistula and a mixed empyema developed in this space. These complications were successfully treated by intercostal drainage and upper thoracoplasty. It is noteworthy that this patient had had pulmonary symptoms since childhood.

Case 2.—The second case* was almost identical to the first. This patient was a college boy, age 18, who was first seen in October, 1938. He was known to have had a lung cyst since the age of 13. This was discovered in a routine roentgenogram at school in 1933 (Fig. 4†). Subsequent films were secured at intervals, one of which, taken in 1937 (Fig. 5), shows the cyst to be empty at that time. The cyst was said to have disappeared at the age of 17. He, however, always had a chronic productive cough which was aggravated by exertion. Two years prior to entering college he had an attack of pleurisy which kept him in bed a week. He never had hemoptysis.

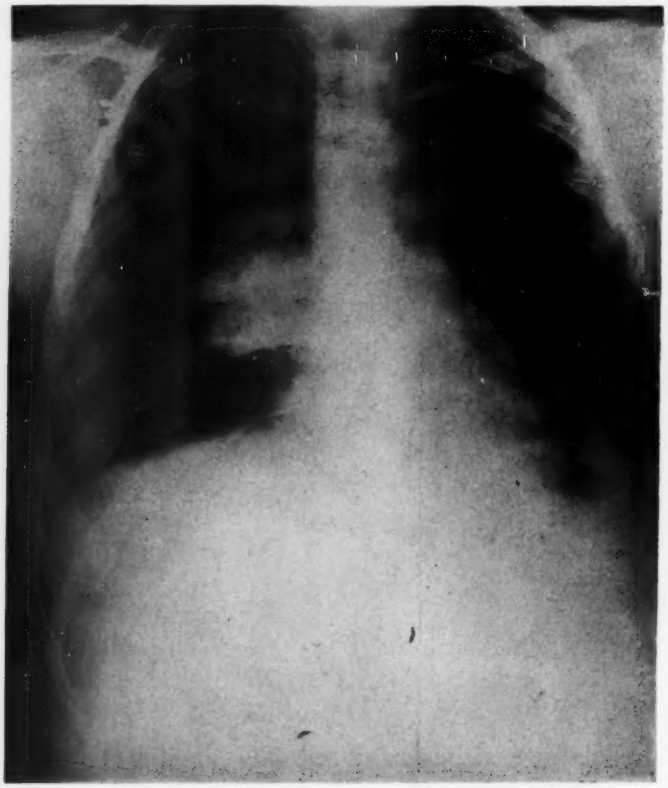

FIG. 4.—Case 2: Appearance of the lungs in 1933, when the patient was 13 years old.

When the boy entered college a routine roentgenogram of the chest was taken, showing a large, thin-walled, sharply defined cavity in the anteromedial portion of the right lung (Fig. 6). The cyst at this time showed a fluid level. He seemed somewhat under par physically, and was easily fatigued. In view of these facts, together with the hazard of harboring such a potentially dangerous lesion, operation was advised. As his home was in Boston, he was referred to Dr. Churchill of the Massachusetts General Hospital.

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* Dr. Edward D. Churchill, of Boston, kindly supplied some of the photographs and clinical data on this case.

† We are indebted to the Massachusetts Department of Public Health for the roentgenograms reproduced in Figures 4 and 5.

He entered the Massachusetts General Hospital, June 26, 1939, where examination of the sputum was negative for tubercule bacilli and *Beta* hemolytic streptococci. Operation was performed, June 29, 1939, and Dr. Churchill was able to dissect the cyst free from the upper lobe without damaging the lobe (Fig. 7). The patient's postoperative course was complicated by the presence of an empyema which required rib resection, but after this his condition rapidly picked up and he was able to finish his college course successfully.

The clinical findings here are compatible with the diagnosis of congenital lung cyst, though the details of the pathologic examination are not at hand.

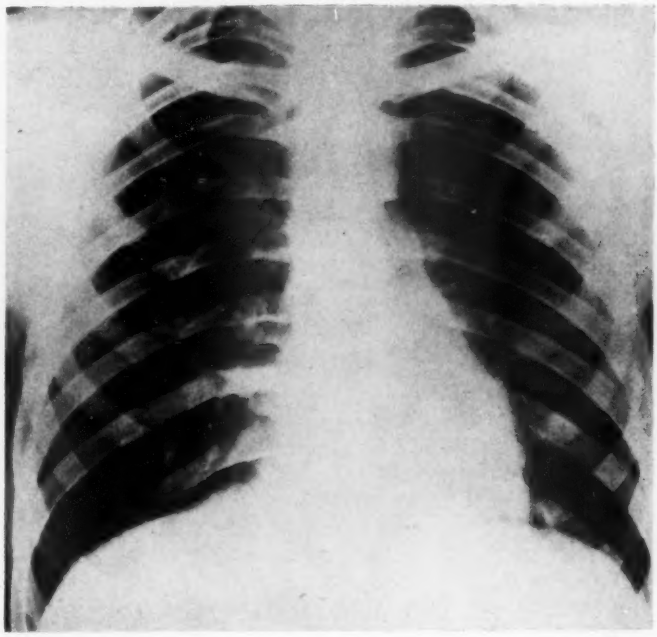

FIG. 5.—Case 2: The cyst now empty. Roentgenogram taken in 1937, when the patient was 17 years old.

SUMMARY: A three and one-half-year postoperative follow-up of this case has been obtained. The patient had a congenital cyst of the right upper lobe with chronic infection and recurrent episodes of acute infection. He made a complete recovery after enucleation of the cyst and subsequent rib resection. A lung cyst was demonstrated in this case roentgenologically, six years before operation. Intermittent pulmonary symptoms had existed since childhood.

Case 3.—This case represents rupture of a cyst causing pyopneumothorax, which occurred in a baby, age three months, who was admitted to the Mary Hitchcock Memorial Hospital for the first time in April, 1941. The baby was very well until ten days prior to admission, at which time she had what was considered to be a gastrointestinal upset, characterized by anorexia, constipation and distension of the abdomen. This cleared up after two or three days but she began to cough and a low-grade

fever was present. One day before admission she began to have paroxysmal attacks of gasping respiration. These attacks were relieved somewhat by propping the baby up on a pillow. On the day of admission there was the sudden onset of gasping respiration, worse than before, and progressive. She was rushed to the hospital *in extremis*, gasping for breath and cyanotic. A roentgenogram taken immediately is shown in Figure 8. It was thought that a spontaneous tension pneumothorax was

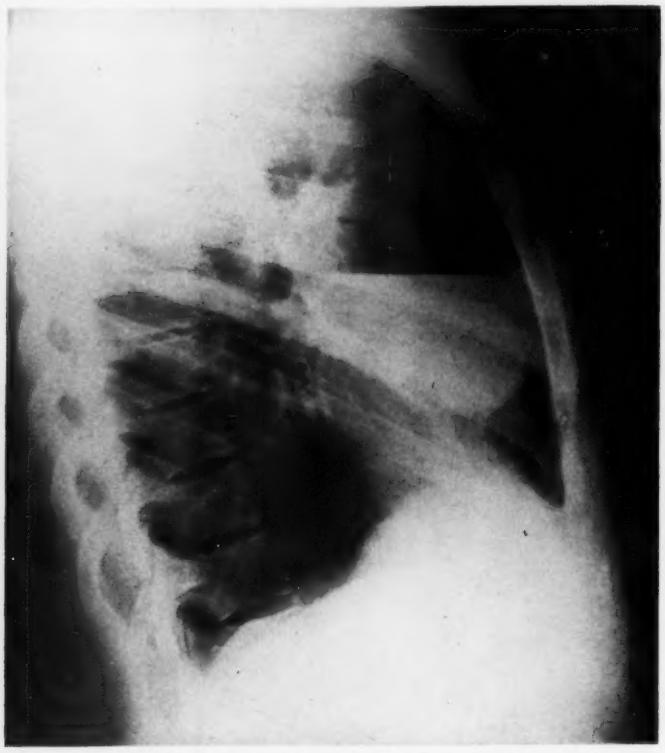

FIG. 6.—Case 2: A lateral view just before operation in 1939.

present, of unknown etiology, though it is interesting to note the clear area over the spine at the base of the right lung field. At once, a needle was inserted in the right pleural cavity and connected with a pneumothorax machine. The pressure was so great that the water was forced out of the monometer and no accurate measurement could be taken. Aspiration of the air was commenced then by syringe, and after considerable amounts had been removed the patient's condition improved. Further aspiration at this time resulted in the withdrawal of thick pus from the right pleural cavity which, on culture, was found to contain pure *Staphylococcus aureus*. The patient's condition was improved by the immediate emergency treatment. Another roentgenogram immediately after the first tap is shown in Figure 9, and demonstrates two definite air pockets. A transfusion was administered because of a rather severe anemia and sulfathiazole was begun.

Several subsequent chest taps were made, which resulted in the withdrawal of thick pus, which always showed a culture of *Staphylococcus aureus*. A later roentgenogram (Fig. 10) demonstrated a definite pyopneumothorax; and as this condition

was gradually relieved, the cystic shadow in the right midlung fields persisted. After three weeks it was no longer possible to aspirate pus from the pleural cavity and roentgenograms failed to show the presence of any residual empyema.

The patient continued to have respirations which were always above 50 per minute, and usually were around 60, occasionally going up as high as 80 or 90. Expansion of the cyst (Fig. 11) was noted with alarm, since it was thought that another rupture might occur at any time. On one occasion the cyst was aspirated with a needle and syringe, and it was found that air was under considerable pressure within the cyst. Following aspiration the cyst was diminished in size, but in 24 hours had increased to its previous dimensions.

In view of the continued elevation of respirations and the progressive expansion of the cyst, it was decided to operate upon the patient, with a view to removing the cyst. An exploratory thoracotomy was performed, July 25, 1941, when the baby was six months old. It was found that the cyst was an extremely thin-walled one, situated between the middle and lower lobes, and densely adherent to both. It was impossible to remove the cyst intact because of the thinness of its walls and the denseness of the adhesions to the surrounding normal lung. It was dissected free piecemeal, and a definite bronchial communication was observed at the hilum. Two silk ligatures were placed around the neck of the cyst close to the hilum and the cyst was cut away. There was practically no evidence of the previous empyema except for avascular adhesions binding the upper and middle lobes to the chest wall, in which was an occasional bit of yellow, grumous material. A Pezzar catheter was placed in the pleural cavity. Immediately upon returning the patient to bed, this was connected with a constant suction apparatus. For the first two or three hours there was difficulty in withdrawing air fast enough by this means, apparently due to a leak through the incision in the chest wall. This sealed off, however, and from here on the patient's convalescence was only complicated by slight difficulty in maintaining the normal chemical balance for the first week postoperatively.

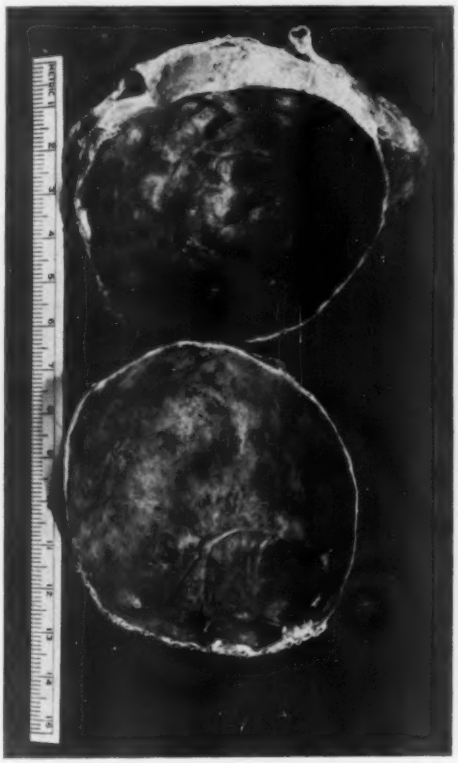

FIG. 7.—Case 2: The surgical specimen was removed by Dr. Churchill, without damage to the lobe.

This undoubtedly represents a congenital cyst. The age of the patient would favor this diagnosis together with the demonstration at operation of a definite bronchial communication. Microscopically, the pieces of cyst submitted for examination revealed small areas of cartilage in the wall and there was one area on the inner surface lined by cuboidal epithelium.

From the location of the cyst in the chest the possibility arises of its having been a cystic accessory lobe. All three normal lobes were accounted for on the right and

the cyst seemed to be independent of all three except for vascular adhesions between it and the adjacent middle and lower lobes.

SUMMARY: A one and one-half-year follow-up has been obtained on this patient, who, at the age of three months, sustained a rupture of a congenital pulmonary cyst on the right side. This resulted in a pyopneumothorax and marked mediastinal shift. The air was immediately aspirated and the empyema cleared up with repeated aspirations and the administration of

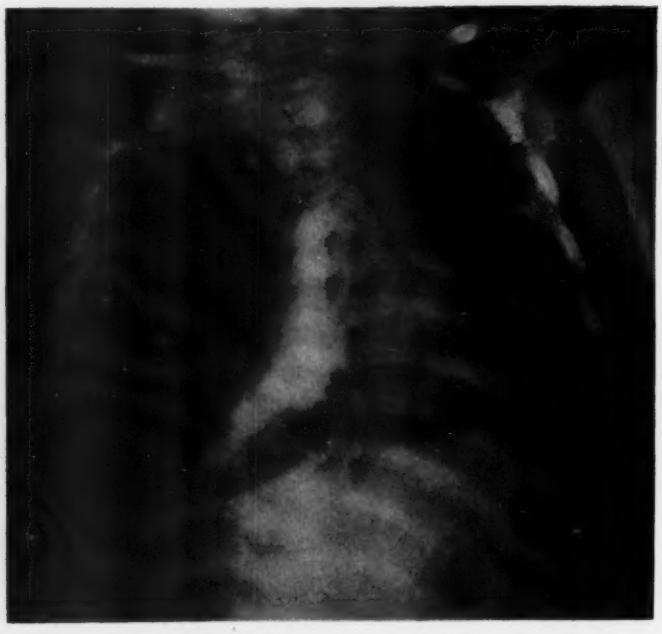

FIG. 8.—Case 3: Chest roentgenogram on admission. There is extreme mediastinal shift. The irregular clear area over the spine just above the diaphragm later proved to be a cyst.

sulfonamides. The cyst then began to balloon up again, and reached huge proportions. When the patient was six months of age the cyst was removed surgically. There is strong evidence in support of the lesion being a cystic accessory lobe.

Case 4.—The following case is one which showed both infection and mechanical difficulties with bronchial air-exchange. The patient was a female, age 36, who was admitted to the hospital, November 24, 1940, with an illness which began six weeks before entry. At that time she began work in a house which was improperly heated, and two or three days after starting work, she became acutely ill, with high fever, diarrhea and soreness of the mouth. Shortly afterwards she developed soreness in the back and extremities, became progressively weaker, and had frequent attacks of sweating. There were no chills. She was taken to a neighboring hospital where, in a few days, the fever subsided somewhat and the soreness of her muscles disappeared. Her strength began to return over a period of two or three weeks, while still in the hospital, until one week prior to entry, when she began to have a paroxysmal cough and afternoon fever. There was also occasional vomiting.

The sputum resembled saliva, and there was no hemoptysis. During this time, also, there was pain in the right upper anterior chest, made worse by coughing and deep breathing.

On admission, the patient appeared acutely ill. Temperature 103° F., pulse 140, respirations 30. Except for emaciation the positive findings were related to the chest. There was tenderness over the right upper anterior portion and diminished resonance over this area. Auscultation revealed diminished breath sounds in front, extending around to the axilla, and numerous moist râles were present. Examination of the rest of the lung fields was essentially normal. One of the roentgenograms of the chest taken on admission is shown in Figure 12.

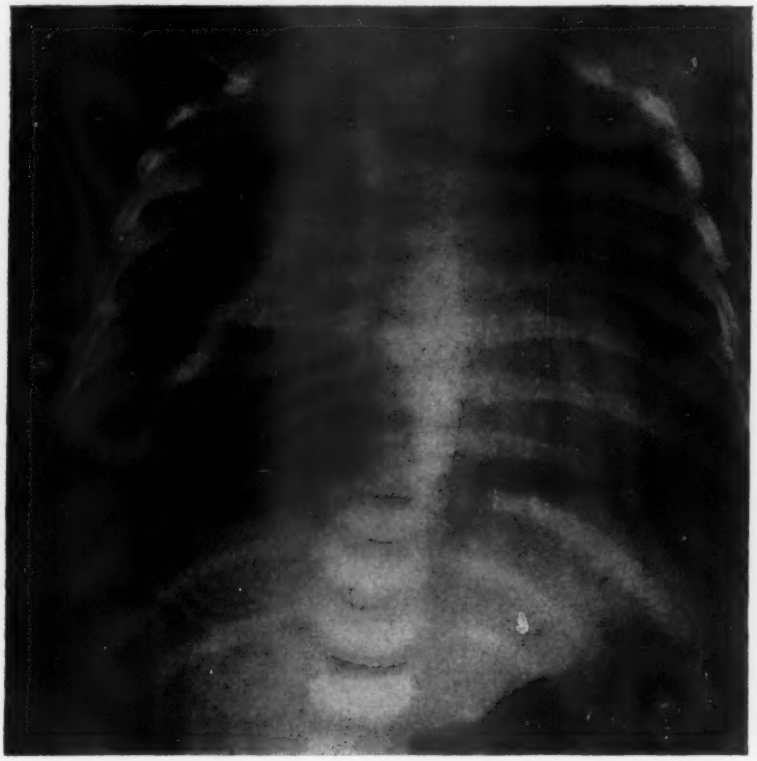

FIG. 9.—Case 3: Picture taken on the same day as Figure 7, after withdrawing air and pus. The cystic cavity is now well outlined.

The diagnosis of lung abscess was made, and it was supposed that this resulted from an earlier pneumonia. Conservative treatment was followed, consisting of postural drainage, bronchoscopic aspiration once a week, and sulfonamide therapy. Several transfusions were administered.

Under this regimen the patient began to improve, and at the end of three weeks her temperature returned to normal where it remained. Her weight, which was not obtained on admission because of the patient's condition, was 92 pounds after she had been in the hospital 17 days. Her weight began to increase during the fifth week of hospital stay, and at the end of 74 days it had reached 101 pounds. The sputum, which on admission amounted to 60 to 90 cc. a day, rose to 240 to 300 cc. as soon as postural drainage was started. During the third week, when the temperature returned to normal, the sputum also dropped to a daily average of 30 to 60 cc.

In January, 1941, after the patient had been in the hospital approximately seven weeks, roentgenologic examination showed a remarkable change in the appearance of the "abscess." As shown in Figure 13, the cavity in the lung was now entirely free of surrounding infiltration, had a very thin wall, and no longer contained fluid. Subsequent examination, two weeks later, as shown in Figure 14, demonstrated an increase in diameter of the cavity.

Possibly the patient had had an infected solitary pulmonary cyst all along, the infection had cleared up, but there was a ball-valve action in the connecting bronchus, with subsequent distension of the cyst. In favor of this hypothesis was the absence

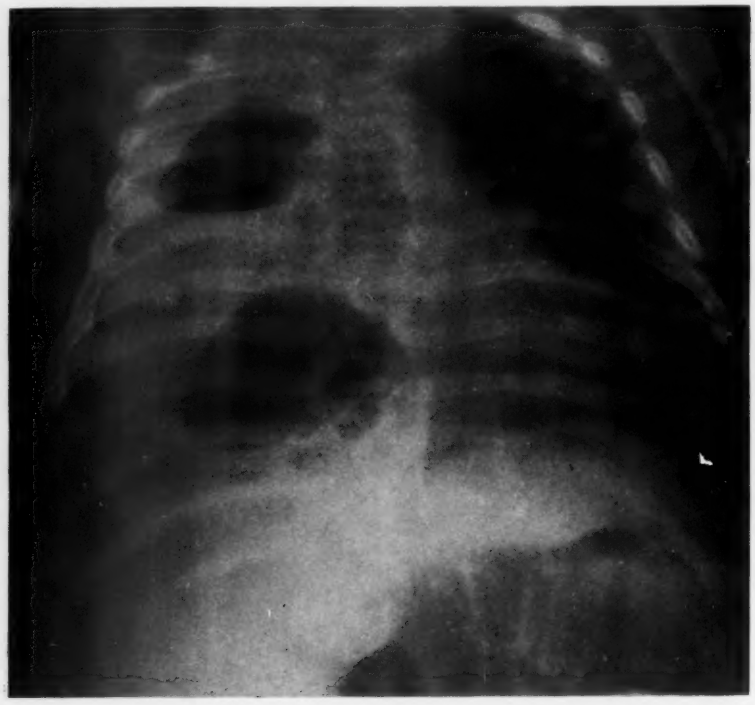

FIG. 10.—Case 3: Roentgenogram nine days after admission showing a pyopneumothorax persisting and the cyst essentially unchanged.

of surrounding pulmonary fibrosis. On the other hand, it is entirely possible that this condition did represent an abscess wherein the infection had cleared and then the bronchus had become partially occluded, resulting in progressive distension of the abscess cavity. There is no clear-cut differentiation between the two conditions in this instance. The importance of the differentiation would be to know whether or not the cyst was lined by epithelium and if the walls contained cartilage. If these were not present, closure could be obtained with drainage, either by open thoracotomy or closed drainage, with a catheter, as pointed out recently by Maier.[5] However, biopsy of the cyst would be necessary to determine this point, and this in itself would require a major operation and drainage would require a two-stage procedure to guard against the development of empyema. Furthermore, biopsy of one portion of the cyst wall would not guarantee a knowledge of the condition of the entire lesion. Therefore, removal of the cyst was decided upon, and, since at this point the patient's condition seemed favorable, operation was performed, February 6, 1941.

A posterolateral incision was made, the scapula was partially mobilized and re-

tracted upward, the fifth rib was widely resected and the pleural cavity opened in the bed of this rib. The cyst of the upper lobe was immediately apparent, lying anteriorly and deeply embedded in the lobe. Where the cyst approached the surface of the lung, there were dense avascular adhesions. The mediastinal aspect of the lobe was adherent also, and the pleural cavity was obliterated over the apex by delicate avascular adhesions. The lower lobe was entirely free and there was no middle lobe present. The cyst failed to collapse with the rest of the lobe when intratracheal pressure was diminished, and firm pressure on the cyst with the hand failed to express any air. It was impossible to remove the cyst separately from the lobe, and in order to remove

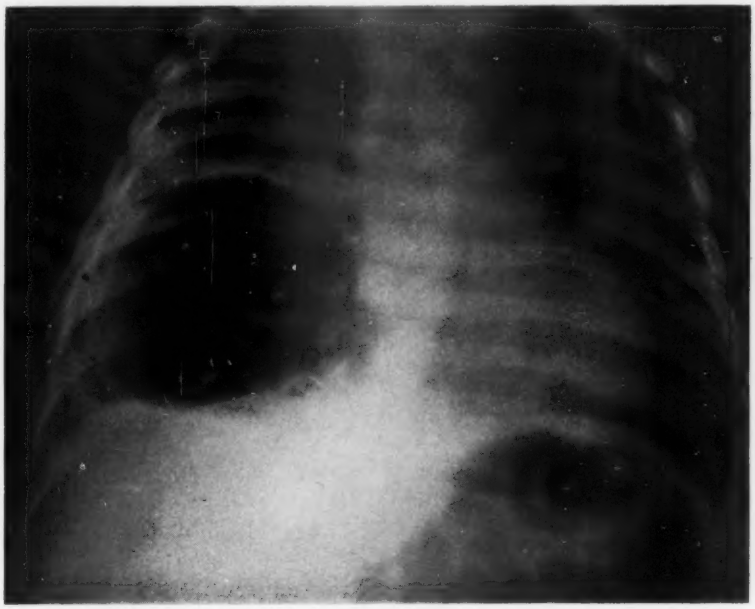

FIG. 11.—Case 3: Three weeks later the empyema has cleared up, but the cyst has expanded to an alarming degree.

the lobe without damaging the cyst, a separate ligation of the upper lobe vessels at the hilum was done. A tourniquet was applied to control the escape of air from the bronchus before the lobe was amputated close to the hilum. A small amount of remaining lung tissue was sutured over the upper lobe bronchus with catgut. The incision was closed without drainage.

The pathologists have not been able to demonstrate a definite bronchial communication with the cyst on gross inspection (Figs. 15 and 16). Microscopically the wall of the cyst was composed of dense, fibrous tissue in which no cartilage was observed. The lining was devoid of epithelium, though it is only fair to state that the cavity was stuffed with cotton before fixation, which could easily have completely denuded a delicate epithelial membrane. Certainly, the necessary and sufficient findings to enable a diagnosis of lung cyst to be made are lacking in this instance and it is probable that lung abscess was the basic lesion.

The patient stood the operative procedure very well and made an entirely uneventful convalescence. Her temperature rose to 101° F. for five days following operation, and then rapidly declined to normal. The lower lobe overexpanded promptly to fill the right thoracic cage except for a small area at the apex which was filled with sterile fluid.

This patient has been followed regularly in the Out-Patient Department and is entirely normal as far as pulmonary symptomatology is concerned. There is still a cap of density over the apex of the right hemithorax, but the patient has no cough and no chest pain, and is able to keep on with her house work.

SUMMARY: A two-year follow-up has been obtained in this case, which exhibited the findings of either lung abscess or infected lung cyst, with progressive ballooning of the cavity. A right upper lobectomy was performed, and the pathologic findings are more in accord with a diagnosis of lung abscess than of cyst. The absence of pulmonary symptomatology prior to the onset of the present illness is against but does not rule out a preexisting cyst.

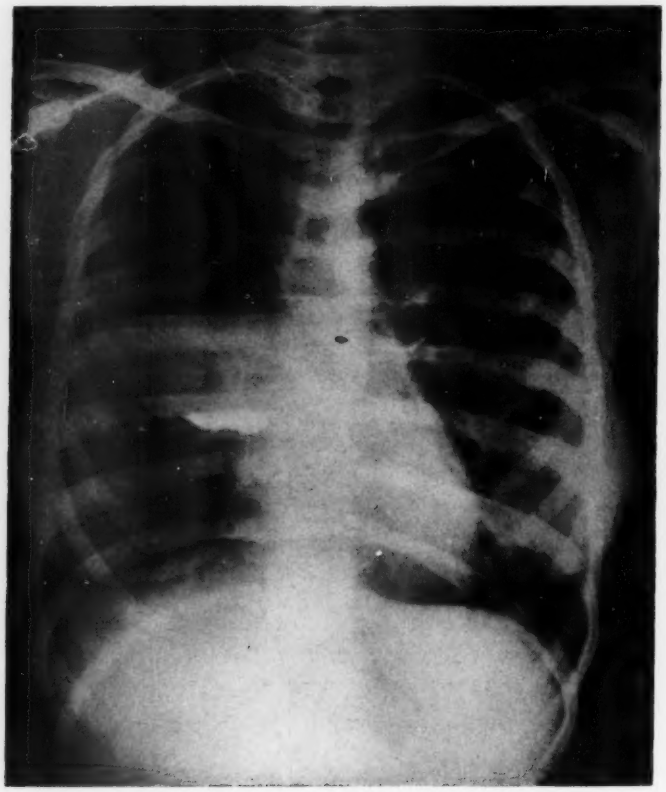

FIG. 12.—Case 4: Chest roentgenogram on admission, when a diagnosis of lung abscess was made.

Case 5.—This case* is characterized by multiple attacks of spontaneous pneumothorax caused by the rupture of a cyst-like structure on the surface of the lung, probably representing an emphysematous bulla.

The patient was a male meat-cutter, age 30, who was first seen March 30, 1936. Two years previously, he had experienced a sudden onset of pain in both sides of the chest and dyspnea. No roentgenograms were taken. The patient gradually improved

* Previously reported in the Jour. Thoracic Surg., 10, No. 5, 566–571, 1941.

and was able to return to work in about two months. A burning, cramping sensation in the right side of the chest persisted for some time. About one year later, he again had a sudden attack of dyspnea and pain, similar to the first. A roentgenogram of the chest, at another hospital, revealed a complete right pneumothorax, with a cyst-like structure projecting beyond the border of the collapsed lung. The symptoms improved rapidly, and the patient returned to work in a week. Three weeks later, he had a third attack, and for some time subsequent to this his physician withdrew air at intervals from his right chest. The third attack lasted four weeks. His symptoms gradually disappeared and he remained well until the middle of March, 1936, when he suffered

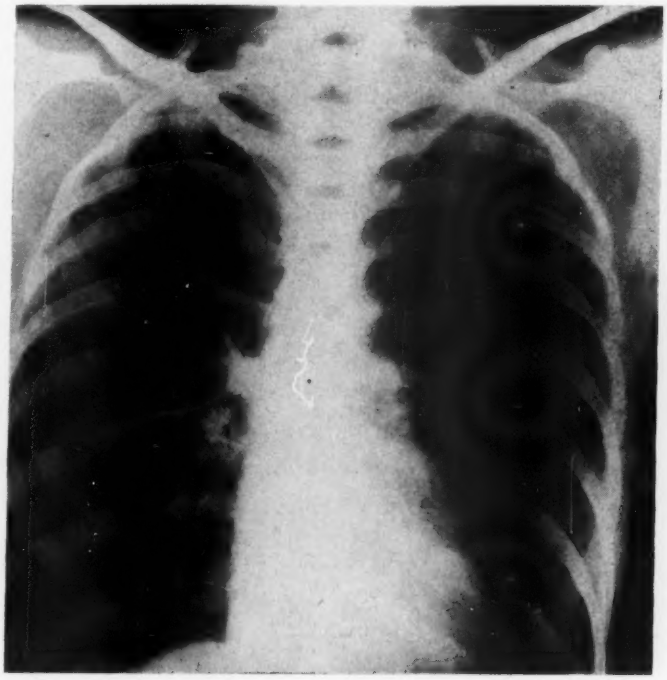

FIG. 13.—Case 4: Five weeks after admission, the clinical and roentgenologic evidence of infection are gone and a cystic shadow remains.

a fourth attack of right-sided chest pain and dyspnea. He was in bed for two weeks, with only partial relief of symptoms. At this time (March 30, 1936) he was referred to the Mary Hitchcock Memorial Hospital.

On admission, the patient presented a picture of extreme dyspnea and cyanosis, with shallow, rapid respirations and weak, thready pulse. The temperature was normal. Physical examination revealed the signs of a right pneumothorax; roentgenograms showed a right tension pneumothorax (Fig. 17). The patient's acute symptoms were relieved by aspiration of air from the right pleural cavity, but repeated aspirations were necessary in order to keep the dyspnea under control. Because it was felt that the adhesions, shown in the roentgenograms, might play some part in preventing closure of the perforation in the lung, thoracoscopy was performed, April 11, 1936, and a cautery pneumonolysis was done, severing the adhesions. Subsequent to this procedure, the patient's condition showed progressive improvement, and the lung partially reexpanded. It was at this time that the large bleb on the right upper lobe was first noted (Fig. 18). The patient was so much improved symptomatically that

he refused to remain in the hospital, and was discharged against advice, April 24, 1936.

He returned to work and felt well until May 15, 1936, when he had a fifth attack, characterized by dyspnea and cyanosis. He was admitted to the hospital, May 16, 1936, in essentially the same condition as on the first admission, except that the symptoms were somewhat less severe. The roentgenogram taken at this time showed a right pneumothorax. Another adhesion had formed.

The emphysematous bleb was considered to be the cause of the pneumothorax, and excision of this lesion was proposed. Justification for this procedure was based on the fact that the frequent recurrences were handicapping the patient, and, also, at least one of the attacks had produced a tension pneumothorax of such alarming proportions that his life was in danger.

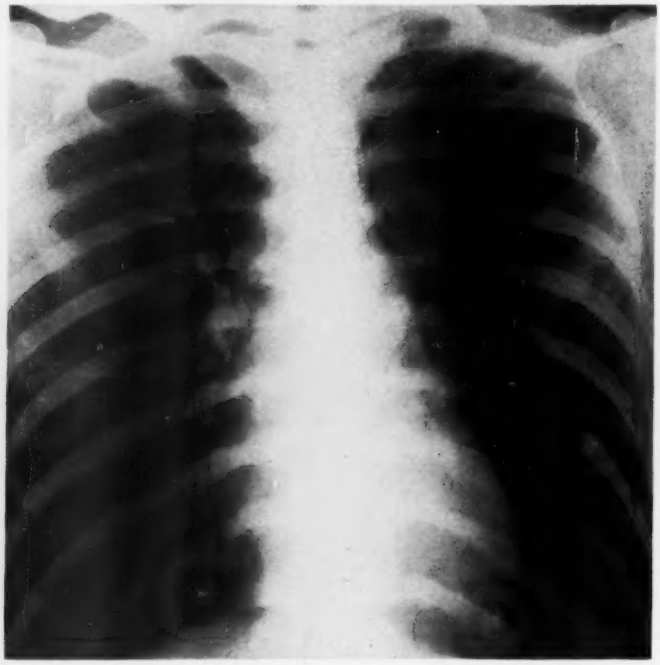

FIG. 14—Case 4: A roentgenogram taken two weeks after Figure 13 shows that the cyst has almost doubled in size.

Operation was performed, May 23, 1936, under intratracheal gas-oxygen-ether anesthesia. A right parascapular incision was made, and the fifth rib was resected. The pleura was incised in the rib bed. A bleb, measuring approximately five centimeters in diameter, was seen on the lateral aspect of the apex of the upper lobe. A broad adhesion extended from the medial aspect and apex of the cyst to the mediastinum. There was a charred area on this adhesion from previous cauterization. There were some adhesions between the middle, upper and lower lobes and some between the lower lobe and the chest wall. The pleural surfaces were otherwise normal in appearance.

The adhesion to the cyst was cut away and hemostasis secured. The apex of the cyst was grasped with forceps, and a purse-string suture was placed in the thickened pleura around the base of the cyst. The suture was drawn tight and the bleb removed.

The cut surface was sewed over, and the incision in the chest wall was closed without drainage.

The pathologic report was as follows: "Study of numerous sections reveals no definitely identifiable lung substance. The only feature suggesting the association of this specimen with the lung is the presence of a great many macrophages filled with black carbon-like pigment. Elastic tissue stains reveal a very small amount of elastic tissue but none in any position to suggest alveolar arrangement. No bronchial structures are seen. Two types of surface are seen in the section; one, which is interpreted as being the original pleural surface, has underlying it a broad band of dense hyalinized fibrous tissue. No covering is apparent, and there is no infiltration of this region.

FIG. 15

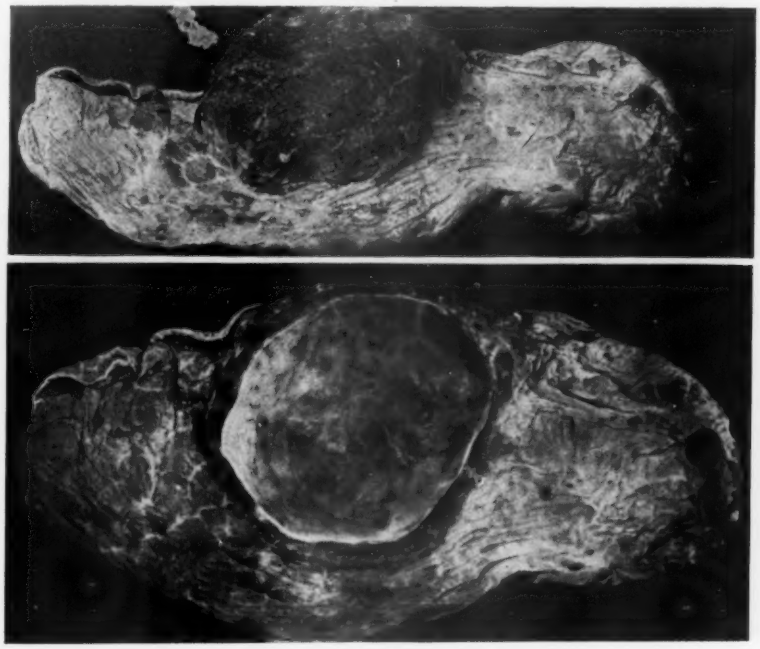

FIG. 16

FIG. 15.—Case 4: The cystic structure is still under tension, though the rest of the upper lobe has collapsed.
FIG. 16.—Case 4: Section of the cyst shows a smooth lining. No bronchial opening is demonstrated.

Opposite this surface is one which bears a small amount of inflammatory exudate in spots. Adjacent to this surface there is abundant infiltration by eosinophils, and a few polymorphonuclear leukocytes and scattered small accumulations of lymphocytes. There are some small arteries which are occluded. Vascular channels are numerous, and there are some brown, pigment-filled phagocytes, suggesting that there has been hemorrhage into the tissues."

Evidence, therefore, is lacking in this case in support of a definite congenital cyst. It probably represents an emphysematous bulla, of the type described by Kjaergaard.[6]

Postoperatively, the patient ran an oral temperature reaching about 100° F. daily for two weeks. The pulse was about 120 for three days and then leveled off to 100, dropping to normal with the temperature two weeks after operation. Respirations were not increased.

During this period there was some mucopurulent sputum. Fluid accumulated in the right pleural cavity, and thoracenteses yielded 350 and 300 cc., respectively, on the 6th and 9th postoperative days. The fluid was serosanguineous, and was sterile on culture.

The patient gradually improved, and was discharged, July 1, 1936. He resumed activities and returned to work. He has now been working seven years as a clerk in a grocery store, with no symptoms or ill effects.

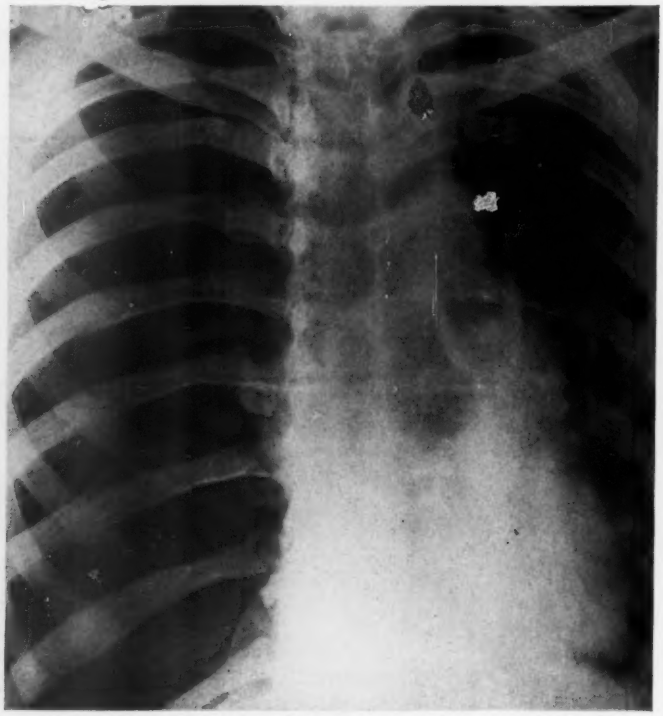

FIG. 17.—Case 5: Roentgenogram taken on admission. There is tension pneumothorax, with extreme mediastinal shift.

SUMMARY: A seven-year follow-up has been obtained in this case, who had five attacks of spontaneous pneumothorax from rupture of a subpleural cyst-like structure. On at least one occasion a high degree of tension pneumothorax was present. The cyst-like structure was excised and the patient has remained well since. Pathologic criteria are lacking for a satisfactory diagnosis of cyst, and it is thought likely that the lesion was an emphysematous bulla.

Case 6.—When first seen for a pulmonary complaint, R. S. was age 24, and was admitted to the hospital, July 15, 1937, with a diagnosis of bronchopneumonia. Routine roentgenograms of the chest demonstrated a small area of acute pulmonary infection in the right costophrenic angle. Also, at this time it was discovered that there was a dense, smoothly-outlined, oval shadow in the left upper lung field (Fig. 19). The patient recovered from the bronchopneumonia promptly, but failed to return for further study of the shadow in the left upper lung field.

He was readmitted in November, 1939, acutely ill and complaining of severe left chest pain, cough and fever. Roentgenograms taken at this time are shown in Figures 20 and 21, and demonstrate a tremendous increase in the size of the previously discovered shadow. While exploratory operation or aspiration of this cystic shadow was being contemplated, the patient had a sudden exacerbation of thoracic pain, became quite cyanotic and breathless. This was soon followed by a diminution of pain in the chest. A roentgenogram (Fig. 22) showed that the cyst had ruptured into the pleural cavity. Thoracentesis at this time recovered 300 cc. of cloudy, thin, yellow

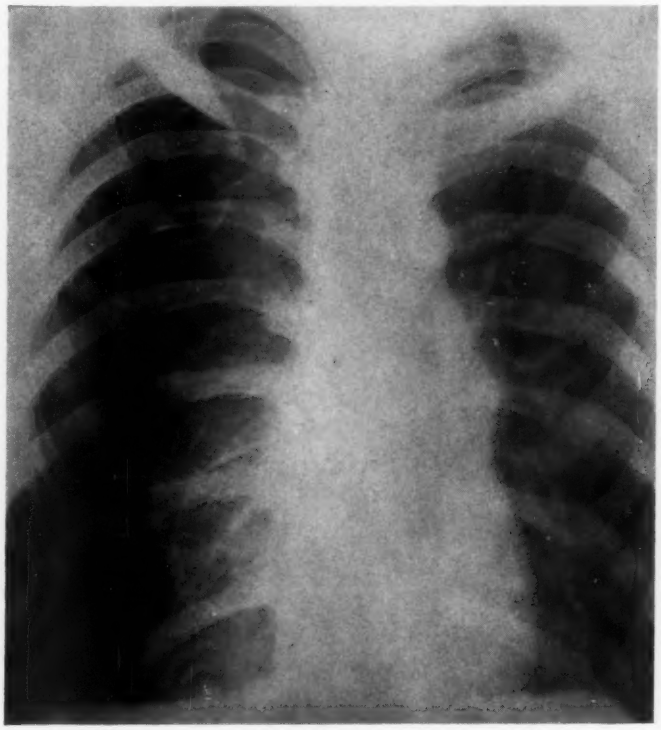

FIG. 18.—Case 5: Partial reexpansion after repeated thoracentesis. The cystic shadow in the upper lobe area is demonstrated.

fluid. Smear and culture were negative for organisms but showed many white cells, most of which were polymorphonuclear leukocytes. Following this episode the patient quickly recovered, his pain disappeared, the temperature returned to normal and he was discharged, after a hospital stay of 12 days.

He returned for operation, June 9, 1940, seven months after his previous admission, and at this time it was seen roentgenologically (Fig. 23) that the cystic shadow had returned to its original size and contour. It is interesting to note in these films an area of increased density at the base of the cystic shadow. Operation was performed June 21, 1940. The left pleural cavity was opened through a posterolateral incision, with resection of the sixth rib. After freeing up a few avascular adhesions, the cyst was easily located protruding through the surface of the upper lobe. It was adherent at its apex to the posterolateral chest wall, and apparently deeply embedded in the lobe. It was possible, however, to develop a cleavage plane between the lung and the cyst, and this progressed without encountering large blood vessels or bronchi. The upper lobe and cyst were completely separated and it was then found that the base of the

cyst was adherent to the arch of the aorta just distal to the left subclavian artery. The cyst was rather thick-walled, and at the base, where it was straddling the aorta, there was a hard mass within the cyst wall. The base was removed from the arch of the aorta without difficulty, complete hemostasis was secured, and the chest was closed without drainage.

The pathologic findings indicate that the specimen represents a cyst of a rudimentary accessory or aberrant lung lobe. The hard area at the base of cyst was found to be a well-formed bronchus, about one centimeter in diameter (Fig. 24). The walls

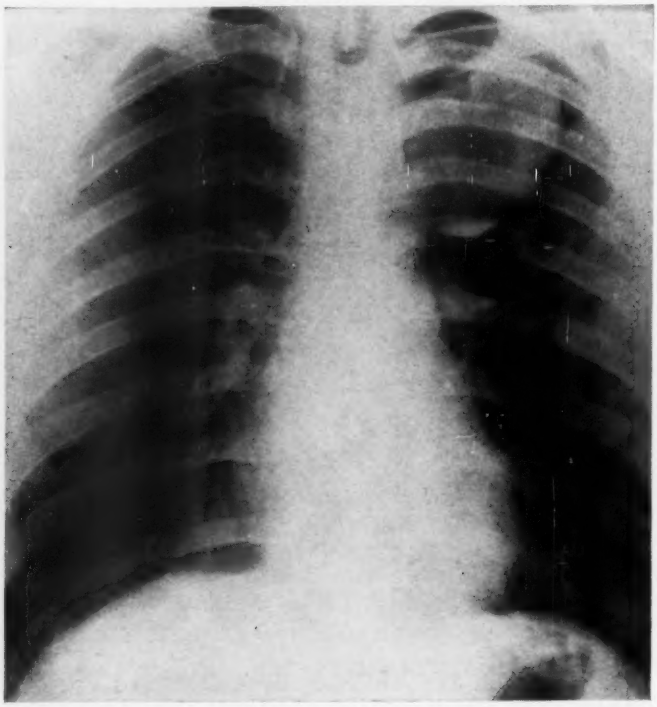

FIG. 19.—Case 6: Roentgenogram taken on admission demonstrates the sharply defined lesion in the left upper lung field. The area of increased density at the base of the lesion should be noted.

contained typical cartilage, and the lining was composed of tall, columnar, ciliated epithelium. The bronchial lumen communicated directly with the main cyst cavity, which measured 7.5 cm. in greatest diameter. The cyst also was lined with columnar, ciliated epithelium.

It is rather difficult to reconstruct the life history of this lesion. The patient had had numerous hospitalizations, here and elsewhere, and no pulmonary lesion had been discovered, to our knowledge. Perhaps originally the rudimentary bronchus was all that existed and, as time went on, the accumulated secretions from the lining epithelium caused a gradual distension of the blind end of the bronchus to form the cyst. The final rapid distension and rupture may have been accounted for by stimulation of the glandular secretion by adjacent or intrinsic infection from which the bacteria had disappeared by the time the cyst ruptured. Examples of similar lesions are infrequent in the literature but disease of aberrant lung tissue was discussed by Freedlander and Gebauer,[7] in 1938.

Convalescence was entirely uneventful. Thoracentesis was performed once, and

sterile, blood-tinged fluid was recovered. The lower lobe gradually expanded to occupy the entire left hemithorax. The patient has been followed at frequent intervals and is entirely free of pulmonary symptoms.

SUMMARY: A two and one-half-year follow-up has been obtained in this case. The lesion represents a cyst of a rudimentary accessory lung lobe which gradually expanded over an unknown period of months or years, with final rupture into the pleural cavity. The fluid obtained was sterile. The cyst arose in the mediastinum and was embedded in the left upper lobe. A definite bronchus was present at the base of the lesion.

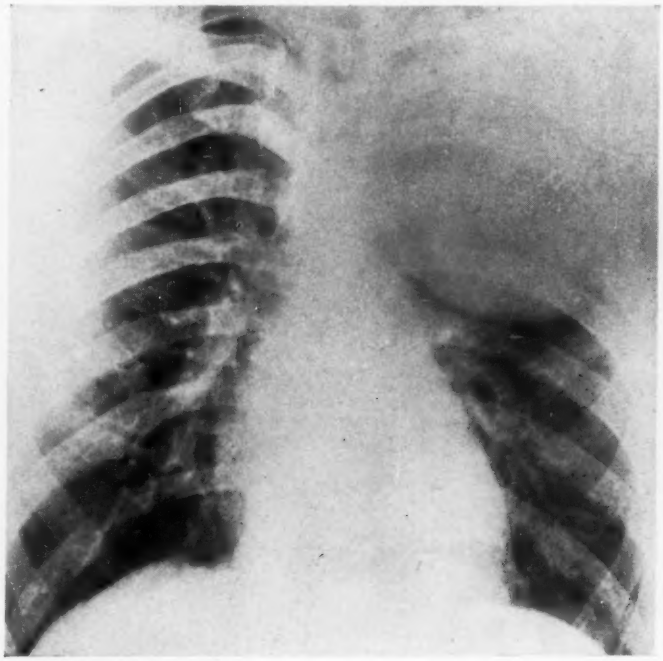

FIG. 20.—Case 6: Appearance of the chest two years and four months after the previous admission.

DISCUSSION

Of the six cases cited, four almost surely represent congenital cysts of pulmonary origin. Two of these (Cases 3 and 6) were cystic accessory lobes arising outside the normal lung tissue. The other two probably were not congenital cysts since one (Case 5) resembled an emphysematous bulla more closely than a true cyst and the other (Case 4) was probably originally a lung abscess, though there are certain findings which militate against this conclusion.

Since all of these cases presented themselves because of acute or subacute manifestations due to the presence of a cyst or cyst-like structure, it is interesting to speculate on the incidence of these structures occurring as silent lesions. A conclusion reached in this regard would help in deciding

the relative danger of ignoring such a lesion when accidentally discovered. Singer[8] states that symptomless cysts are not often seen, and believes they probably should not be operated upon. Eloesser[9] and Maier,[10] also, are of this opinion, and the latter believes that many so-called upper lobe cysts are the result of infection and are not true cysts.

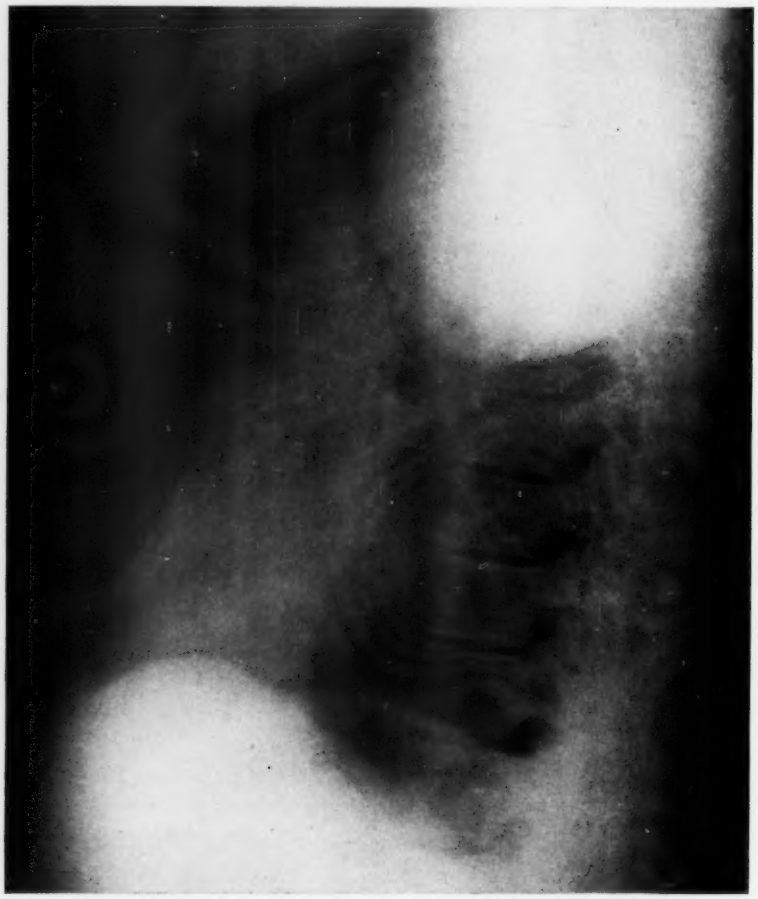

FIG. 21.—Case 6: A lateral view shows the posterior position of the lesion.

A review of the findings on routine roentgenograms taken on all members of the entering class at Dartmouth College reveals that in the five years between 1935 and 1942, 4,983 examinations were made. The diagnosis of solitary lung cyst was made once, and that is our Case 2. This could not be considered an accidental finding nor a silent lesion since the patient was known to have a cyst and it had been productive of symptoms for years. During the same years in the general hospital, 6,622 chest roentgenograms were taken, including retakes; and one unquestionable instance of an asymptomatic lung cyst was encountered.

This occurred in a woman age 56, who entered the hospital for removal

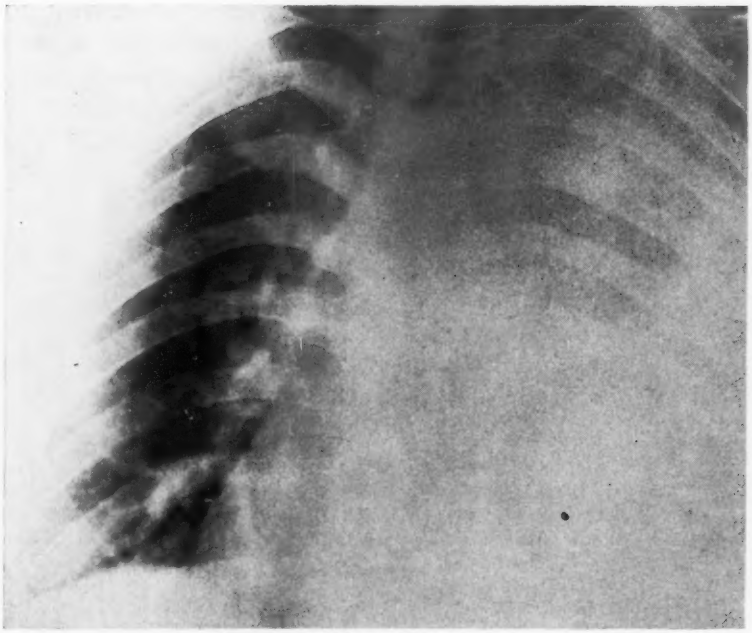

FIG. 22.—Case 6: The cystic lesion has ruptured into the pleural cavity.

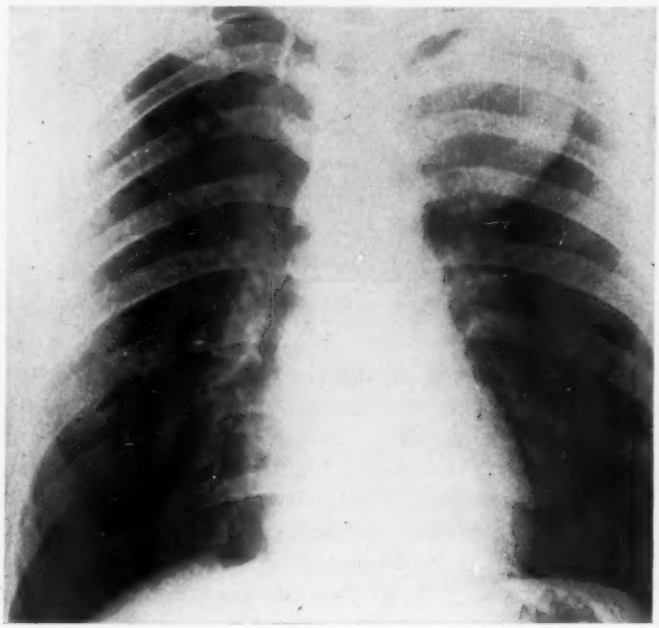

FIG. 23.—Case 6: Six months after rupture the cyst has resumed its original contour.

of a toxic adenomatous thyroid. The lateral chest roentgenogram is shown in Figure 25. The patient was an intelligent, educated woman, and had consulted her physician at regular intervals. She had no knowledge of the existence of any lung lesion, and there was no history of pulmonary difficulties. She had an uneventful convalescence from subtotal thyroidectomy, under local anesthesia, performed July 27, 1937, by Dr. J. P. Bowler. A letter

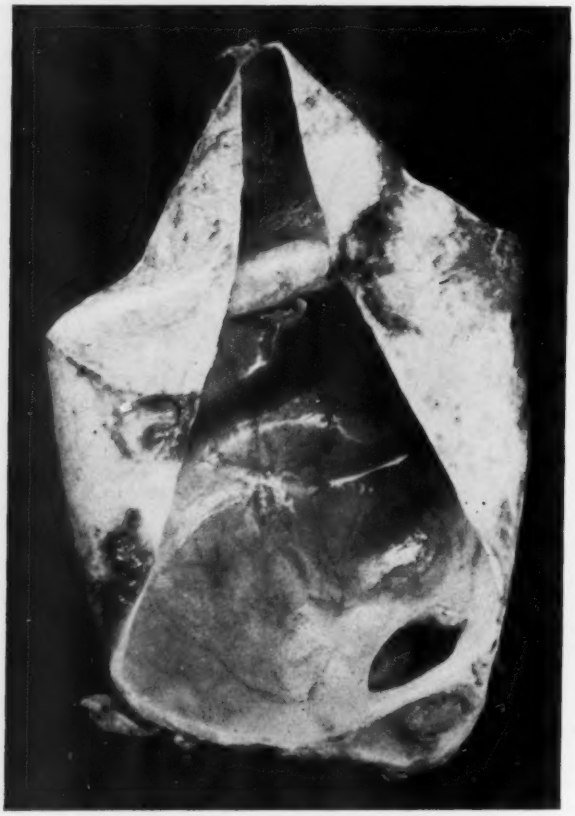

FIG. 24.—Case 6: The opened surgical specimen showing the well-formed bronchial stump at the bottom of the cyst.

received from her, dated June 25, 1942, states that she has been in perfect health since her hospital stay, and there have been no pulmonary symptoms of any kind.

There was one other case which might be a pulmonary cyst, but the diagnosis is so uncertain that it is not included in the present report.

From this small number of roentgenograms, and from accounts in the literature, as cited above, it would seem that asymptomatic cystic pulmonary lesions must be uncommon, but, in contrast to some other opinions, we feel that when they are observed removal should be advised if the patient's condition will permit. The likelihood of accidents to the lesion is very

great, and once complications have occurred a serious situation may develop rapidly and, at best, an extremely eventful clinical course may readily ensue.

Extirpation of the lesion, when possible, would seem to be the best method of treatment. If the lesion has an epithelial lining, collapse or simple drainage will not effect a permanent closure of the cavity (cf. discussion under Case 4). The scope of the operation may vary from simple excision or enucleation of the lesion itself, as in three of the cases herewith reported,

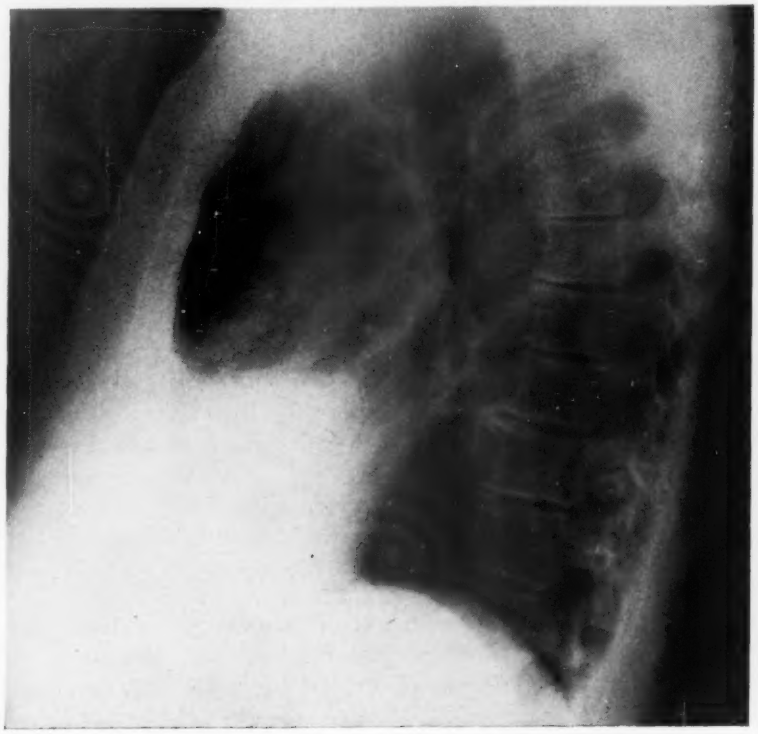

FIG. 25.—Case cited in Discussion: A thin-walled cyst in the left anterior lung field; fluid level at bottom.

or lobectomy, or even total pneumonectomy may be required (Gale,[11] Roberts,[12] and others). Three cases reported by Maier and Haight,[13] were first treated as empyema by open drainage, but due to failure of cavity closure, later lobectomy in two cases, and enucleation in the third, were required for cure. Permanent closure of large balloon cysts by an endocutaneous flap is discussed by Brown and Brock.[14]

The elimination of infection in the cavity inasfar as possible is an important preoperative requirement. With a bronchial communication, postural drainage may accomplish this goal, but in closed cysts or where the communicating bronchus is inadequate due to its small diameter, or its position relative to the cavity, external drainage may be required as in the cases of Maier and Haight, cited above. Since the cyst contents or lining may harbor pathogenic

organisms even under the best circumstances, avoidance of opening the cyst during removal is desirable, but is an ideal not always possible of achievement. To remove the cyst intact, careful dissection and individual ligation of the hilar structures may be necessary. This technic was employed successfully in one of our cases (Case 4) and, if it had been utilized in Case 1, instead of the tourniquet technic, opening of the cyst, and possibly the following empyema, might have been avoided.

The employment of drainage after cyst removal is, of course, an individual problem and one that has to be settled at the time, but, in general, it is probably a safe maxim that, if the cyst has been opened during removal drainage should be instituted.

The postoperative care of this class of patient does not employ different management from that utilized after other open chest operations where there has been manipulation or actual resection of lung tissue. Prompt expansion of the remaining pulmonary tissue should be accomplished and maintained. Whether or not to increase the oxygen intake depends on the individual situation and may be unnecessary. The usual attention must be given to fluid intake and blood replacement. Even if no lung tissue is resected, there is usually an accumulation of serosanguineous fluid in the pleural cavity in the first 48 hours. If no drainage has been employed, aspiration of this fluid once or twice may be advisable, more for bacteriologic determination than relief of pressure. If there is no infection the fluid will absorb over a period of 10 to 14 days.

Complete restoration of the pulmonary function should be the rule, and has been accomplished in all of the cases reported in this article.

SUMMARY

Seven cases of solitary cystic lesions of pulmonary origin are reported. Six of these cases presented themselves for treatment because of various accidents incident to the presence of the cyst. All six were operated upon successfully (five by the author). The seventh case had a symptomless cyst and has not been operated upon. The incidence, diagnostic criteria, operative procedures and pathologic findings relating to these lesions are discussed.

CONCLUSIONS

1. Solitary cystic lesions are usually seen because of some accident to the cyst.

2. The cure of the condition is usually surgical and preferably involves extirpation of the cyst, which may require lobectomy or pneumonectomy.

3. The differentiation between congenital and acquired cysts prior to pathologic examination is often impossible.

4. Symptomless cysts are uncommon.

5. Even silent solitary cystic lesions should be removed if conditions permit.

The author wishes to express his thanks to the Thoracic Study Unit of the Hitchcock Hospital for their cooperation in caring for the cases reported in this article.

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THE SPREAD OF CARCINOMA OF THE RECTUM: INVASION OF LYMPHATICS, VEINS AND NERVES*

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SINCE THE WORK OF HANDLEY,[15] in 1910, much attention has been given to the lymphatic route of spread of carcinoma of the rectum. Many extensive and painstaking studies have been made into this feature of rectal carcinoma in order to determine the prognostic implications of nodal involvement and the direction of spread of the carcinoma. The anatomic descriptions of the rectal lymphatic channels by Delamere, Poirier and Cuneo[9] paved the way for later studies. Early investigations by Miles,[22] Monsarrat and Williams,[24] Cole,[5] Cheatle,[4] Pennington,[29] and others, gave impetus to more exhaustive studies by McVay,[21] one of us (Bargen[2]) and Larsen, Gabriel, Dukes and Bussey,[12] Gilchrist and David,[13] Coller, and others,[6] and Grinnell.[14] These investigators, and the large numbers of cases studied by them, have emphasized the importance of the lymph nodes as prognostic indicators in rectal carcinoma, and around this pathologic feature of the disease have been centered the present methods of surgical treatment.

Venous invasion in rectal carcinoma has been observed for many years, Mayo,[19] McArthur,[20] Smith,[30] Monsarrat and Williams,[24] and Miles[23] noting this feature and commenting on it. During the past four years, increasing attention has been given to venous invasion of rectal carcinoma as its clinical and prognostic importance has been seen to grow. The frequent development of visceral metastatic lesions after radical resection of the rectum for carcinoma has stimulated interest in this phase of invasion by carcinoma.

Brown and Warren,[3] in one of the first reports during the present period of interest, expressed the opinion that the lymph nodes have been poor indicators of visceral metastatic lesions, which are often present independently of neoplastic nodes. They found that 31 per cent of patients without nodal involvement by carcinoma had visceral metastatic lesions, and they maintained that the spread of rectal carcinoma through the blood vessels is at least as important as by the lymphatic route, and that evidence of this spread is usually available in the primary growth. In the prediction of visceral metastatic lesions from the primary growth, the presence of intravascular invasion means as much from the prognostic standpoint as neoplastic nodes, and its absence means much more.

* Abridgment of thesis submitted by Dr. Seefeld to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of M.S. in Surgery.

Dukes and Bussey found that in 16.6 per cent of 699 specimens of rectal carcinoma the veins were invaded and demonstrated small carcinomatous implants along the superior hemorrhoidal vessels.

Grinnell recently found veins involved in 36 per cent of 75 cases studied. In 90 per cent of 30 cases in which there were visceral metastatic lesions, venous invasion was demonstrated in the primary growth. Twenty-five per cent of the patients who had visceral metastatic lesions failed to show nodal involvement.

The first reported instance of neoplastic invasion of nerves was probably that of Cruveilhier,[8] in 1842, but this phenomenon has been encountered frequently since then, and almost all types of neoplasm have been observed to use the perineural spaces as a route of extension. Excluding reports of isolated instances of perineural invasion, no exhaustive investigation of invasion of nerves had been undertaken until 1936 when Warren, Harris and Graves[32] were struck with the frequency of its occurrence in prostatic carcinoma. Kahler,[16] in a later study, placed perineural invasion at the head of the list of criteria for the microscopic diagnosis of prostatic carcinoma.

As early as 1770, Cotugno[7] described spaces about the sciatic nerve which he demonstrated in the cadaver. Other investigators followed with studies to determine the anatomic nature of these spaces and the presence or absence of a definite communication with the spinal subarachnoid space. Key and Retzius,[17] Orr and Rows,[25-28] Weed,[33-36] Alford and Schwab,[1] and Sullivan and Mortensen[31] have contributed greatly through injection experiments on man and animals, to the knowledge of the nature of the neural spaces and of the direction of flow of the fluid therein.

The fact that these spaces exist about the nerves to their smallest ramifications, and that there is a circulating fluid medium within, gives rise to the contemplation of another possible mode of spread of neoplastic cells, and thus suggests a possible relation between recurrence and metastatic spread of a malignant growth and perineural invasion. This feature has been noted in rectal carcinoma but there has been little or no mention made in published reports of its possible relation to the recurrence and visceral spread of rectal carcinoma.

This study concerns itself with the incidence of perineural invasion in a series of cases, along with that of venous invasion and nodal spread, and an attempt to correlate their presence with available clinical data.

METHODS AND MATERIALS

One hundred gross operative specimens of rectal carcinoma removed by the abdominoperineal or the abdominal route at the Mayo Clinic, during the year 1935 and the early part of 1936, were chosen for study in the order of their removal. Specimens removed during these particular years were chosen so that a sufficient interval for adequate follow-up study of the patients who had the growths might have elapsed.

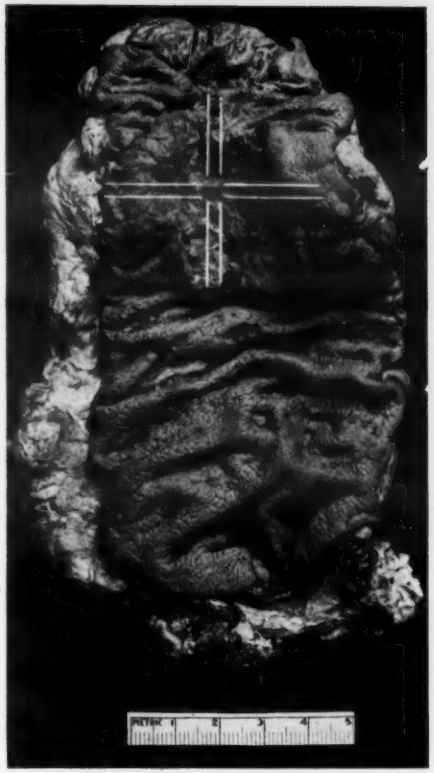

FIG. 1.—Surface view of lesion after bowel had been opened, showing location of blocks removed from each of four quadrants.

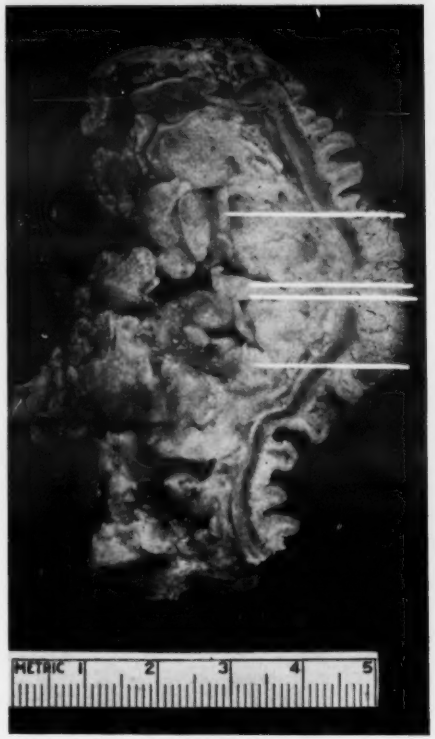

FIG. 2.—Cross-section showing depth of blocks from the four quadrants. Normal mucosa and perirectal tissue included in each block.

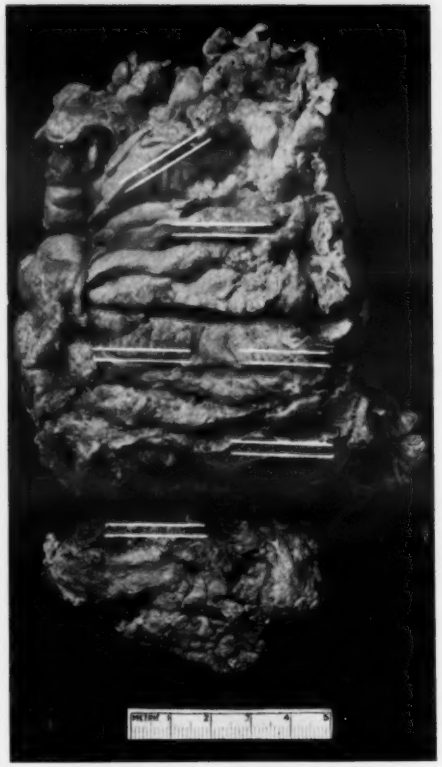

FIG. 3.—Posterior view showing cross-cuts and location of blocks removed in search of venous and perineural invasion. Blocks extend through the perirectal tissue to the intestinal wall.

To study the involvement of veins, blocks of tissue from all points of the lesion and rectal wall at which microscopic evidence of venous invasion could conceivably be present were removed. The lesion was divided into four quadrants and a block of tissue was taken from each quadrant. The block included the full-thickness of the lesion and the entire thickness of the rectal wall as well as a certain amount of perirectal tissue (Figs. 1 and 2). In addition, transverse cuts were made through the perirectal fatty tissue, exposing the larger vessels leading from the vicinity of the lesion (Fig. 3), and blocks were removed for microscopic study from regions which appeared suspicious, usually within a distance of four inches (10 cm.) above and below the growth.

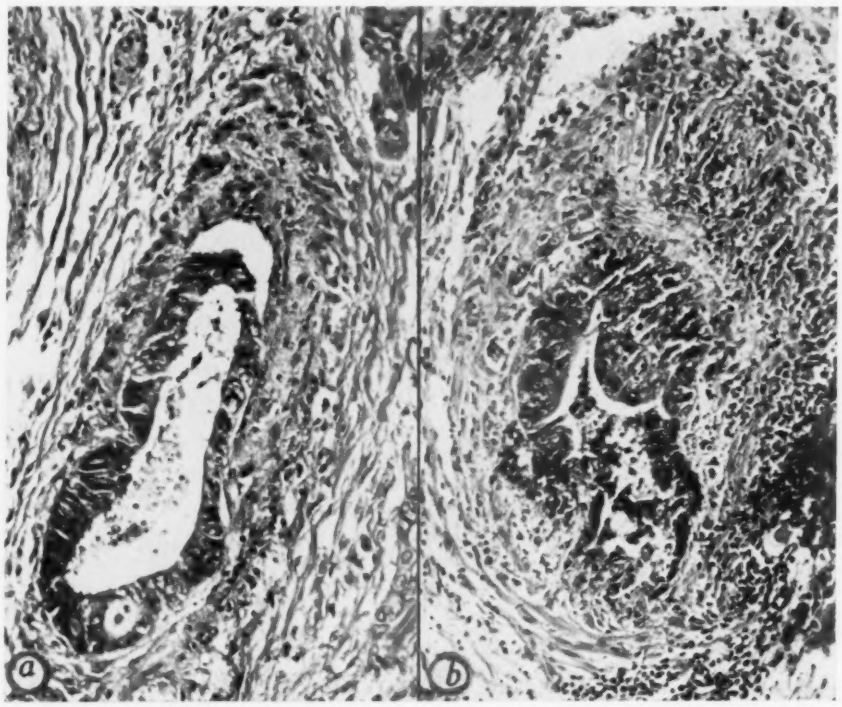

FIG. 4.—(*a*) Photomicrograph of small vein in the perirectal tissue; the lumen is lined by malignant cells (× 185); (*b*) adenocarcinoma, Grade 4. (Broders' method), in the lumen of a small vein in the perirectal tissue (× 140).

Preliminary microscopic examination of sections cut from the blocks, fast freezing technic being used, was facilitated by the use of an acid polychrome methylene blue stain, which is especially adaptable for tissues that have been long fixed in formalin. Of those tissues in which definite or presumptive evidence of venous or perineural invasion was found, permanent sections stained with hematoxylin and eosin were made and further study was carried out. We wish to thank Dr. MacCarty, in whose laboratory the study was made, and Dr. Dockerty, who reviewed the sections.

After examination of all sections was completed, results were tabulated and correlation with clinical data and follow-up records was attempted.

In this method of study, as in others reported to date, there were a few cases in which it was extremely difficult to distinguish small submucosal lymphatic channels from venous channels, and in these cases van Gieson's stain was employed with some degree of success. The presence of erythrocytes within the lumen of a vessel may often aid in distinguishing the type of vessel, but it must be borne in mind that hyaline and necrotic

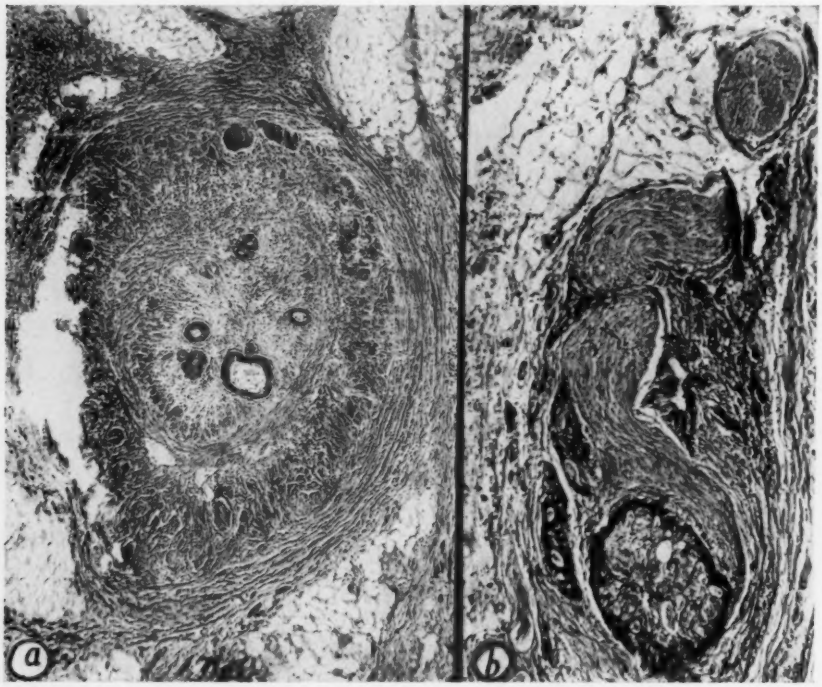

FIG. 5.—(*a*) Photomicrograph showing malignant canalization of a thrombus in a large vein in the perirectal tissue (×35); (*b*) invasion of perineural spaces by colloid adenocarcinoma, Grade 2, showing formation of alveoli and secretion of mucus. Note uninvolved nerve nearby (×60).

material may closely resemble erythrocytes, and also that lymphatic channels may contain erythrocytes as a result of trauma or the surgeon's knife. The presence of smooth muscle, as demonstrated by van Gieson's stain, is of some help.

Most of the involved veins were found in the perirectal tissue near to the muscle wall or within the perirectal fat (Figs. 4 *a* and *b* and 5 *a*). There were no instances of invasion of an arterial lumen, a fact that emphasizes the oft-mentioned immunity of these vessels to carcinomatous invasion. Perivascular lymphatic vessels were seen to be involved, but there was no penetration of the arterial wall.

An interesting feature noted was the frequency of arterial thrombosis in cases in which the veins were involved. This occurred in a number of

instances, and when seen on preliminary examination was taken as an indicator of venous involvement.

In arriving at the final microscopic diagnosis, we considered only cases in which the involved vessels were definitely venous and eliminated all cases in which the observations were indefinite.

Perineural invasion is not as difficult to recognize as is involvement of venous channels. In most instances, involved nerves are abundant in the section, although by no means all of the nerves in one section are always involved. Many fields were examined in which a nerve was seen to be extensively involved whereas one or several nerves in the immediate vicinity were not involved (Fig. 5 *b*). Invasion of nerves was seen as far as four inches (10 cm.) from the site of the primary growth.

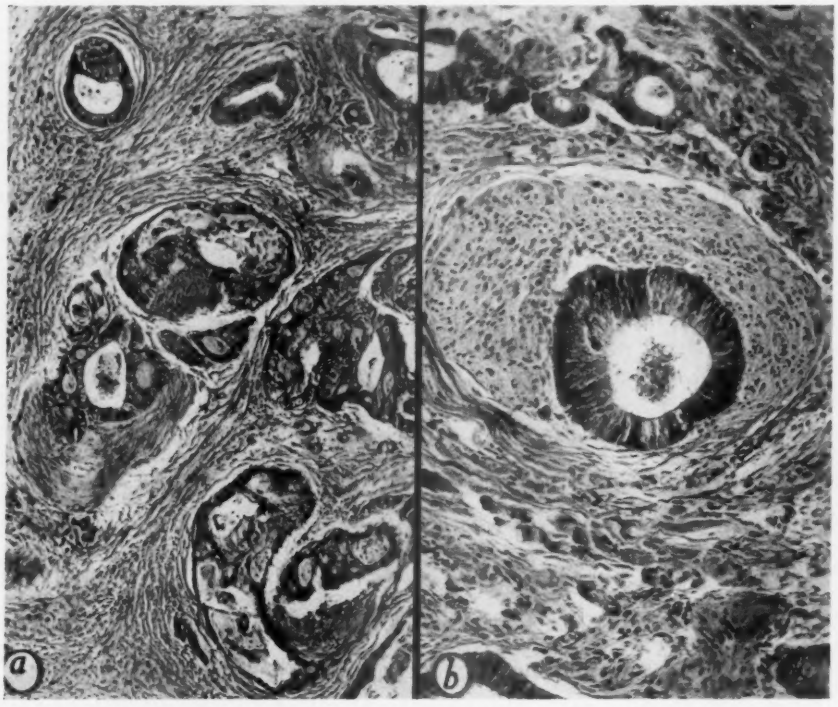

FIG. 6.—(*a*) Photomicrograph showing extensive invasion of nerves with marked distention of the neural spaces, and formation of alveoli (×70); (*b*) showing alveolus in the endoneural space with compression of the surrounding nerve fiber, but without degeneration of the nerve (×125).

Many cases were rejected because of "secondary" involvement of nerves. This was usually present in nerves close to the lesion. The nerve was completely surrounded by extensive carcinomatous infiltration but the perineural space remained intact and did not contain carcinoma cells within its confines, indicating that the nerve was merely isolated by surrounding carcinoma and not actually invaded.

Involvement of the perineural space varied in architecture. In some instances a few malignant cells were seen lying within the space without

any apparent conformation, while in other cases the cells were arranged in alveoli and even distended the space with their mucous secretion (Fig. 6 *a*).

There was little or no degeneration of nerve fibers to be seen in the nerves involved, apparently because of the distensibility of the walls of the perineural spaces, which were seen to be extremely distorted in places (Fig. 6 *b*).

In no cases were the plexuses of Meissner and Auerbach seen to be involved, although nerve fibers both proximal and distal to these structures might be invaded.

RESULTS

Lymphatic Involvement.—Involvement of the lymph nodes was found to be present in 47 per cent of the 100 cases. In previous investigations based, in total, on more than 500 specimens, the proportion of cases in which lymph nodes were involved varied from 36 to 68 per cent (Table I). We found,

TABLE I

NODAL INVOLVEMENT FOUND IN PREVIOUS STUDIES

Author	Total No. of Cases	Percentage Involved
McVay	100	47
Wood and Wilkie[37]	100	51
Gabriel, Dukes and Bussey	100	62
Gilchrist and David	25	68
Coller, Kay and MacIntyre	53	64
Grinnell (1916-1932)	107	36
Grinnell (1938-1941)	75	55

as others before us, that the higher the grade of malignancy (Broders' method) the higher the incidence of nodal involvement (Table II).

TABLE II

INCIDENCE OF NODAL, PERINEURAL AND VENOUS INVASION ACCORDING TO GRADE OF MALIGNANCY (BRODERS)

		Nodal Involvement		Perineural Involvement		Venous Involvement	
Grade	Total Cases	Cases	Percentage	Cases	Percentage	Cases	Percentage
1	14	3	21.4	2	14.3	1	7.1
2	54	20	37.0	16	29.6	7	13.0
3	24	18	75.0	9	37.5	7	29.2
4	8	6	75.0	3	37.5	5	62.5
Totals	100	47		30		20	

Dukes[10] expressed the opinion that metastatic growths in lymph nodes are more frequently found among women than among men, a feature which is not borne out in this study, 46.1 per cent of women and 47.5 per cent of men having nodal involvement.

Dukes has stated that the highest incidence of nodal involvement occurs among young patients, while the tendency is less frequent among the older patients. This fact was also noted in this series (Table III).

Most investigators, notably Mayo and Schlicke,[18] have found the highest

incidence of nodal invasion in the upper part of the rectum and in the rectosigmoid. In this series a slightly higher proportion of nodal involvement was found in the middle third of the rectum than in the other segments, 50 per cent in the middle third, and 48.8 and 40.2 per cent in the upper and lower thirds, respectively.

Of the series of patients who had nodal metastatic lesions, ten patients survived for three years while only two survived for five years.

Perineural Invasion.—Involvement of the perineural and endoneural spaces was demonstrated in 30 of the 100 cases, the average age of the patients who had perineural involvement being 51 years, almost exactly the average age in the entire series. Eighteen of the 30 patients were men (60 per cent), and 12 were women (40 per cent).

The average preoperative duration of symptoms among those patients who had involvement of nerves was 9.4 months, as compared with 9.7 months in the entire series. Pain was a prominent symptom, volunteered by the patient, in 24 cases; it was not mentioned in the history of three cases; and was stated

TABLE III

INCIDENCE OF NODAL, PERINEURAL AND VENOUS INVOLVEMENT ACCORD NG TO AGE

		Nodal Involvement		Perineural Involvement		Venous Involvement	
Age, Years	Total Series	Cases	Percentage	Cases	Percentage	Cases	Percentage
20-39.....	11	7	63.6	3	27.3	4	36.4
40-59.....	68	34	50.0	21	30.9	13	19.1
60-79.....	21	6	28.6	6	28.5	3	14.3
Totals.....	100	47		30		20	

to be absent in three cases. Thus, in 89 per cent of the cases in which information on this point was available, pain was a prominent symptom. In the evaluation of pain in this study, only cases in which the history indicated that the pain might be directly neurogenic and not just discomfort vaguely noted by most patients with rectal carcinoma, were recorded. Terms such as "aching," "boring," "gnawing," "constant" or "steady" were considered to be indicative of pain due to involvement of nerves, while tenesmus, cramps, a feeling of fullness and the desire to defecate were not so considered. Of the 70 cases in which the nerves were not involved pain was found to be a primary symptom in only 25. Pain was not mentioned in the history of 20 cases, and in 25 cases, when the patient was questioned, he stated that it was definitely absent or was present in one form or another but not localized to the rectum. The incidence, then, of pain for cases without perineural involvement in which information was available was 50 per cent.

Of the 30 cases in which there was involvement of the nerves, the lymph nodes were also involved in 20 (67 per cent).

When involvement of nerves was considered in the light of grading, both by cellular differentiation (Broders) and by mural penetration (Dukes), it was seen that the higher the degree of malignancy, the more frequently was perineural involvement present (Tables II and IV).

TABLE IV

INCIDENCE OF PERINEURAL AND VENOUS INVASION ACCORDING TO DEGREE OF MURAL PENETRATION (DUKES)

	Perineural Involvement		Venous Involvement	
Class	No. of Cases	Percentage of Involved Cases	No. of Cases	Percentage of Involved Cases
A	0		0	
B	10	33.3	3	15
C	20	66.7	17	85
Totals	30	100.0	20	100

There is no apparent relation between the size of the carcinoma and the presence of perineural invasion.

In considering the presence of perineural invasion in relation to the location of the growth, it seemed feasible to divide the rectum into lower, middle and upper thirds, including lesions of the rectosigmoid in the latter group. It was found that lesions exhibiting involvement of the nerves occurred equally in the three locations (ten cases in each third), so that the presence of perineural invasion is apparently not related to the location of the lesion. This result contrasts with involvement of lymph nodes, which, in this series, was more frequent in the middle and upper thirds of the rectum than in the lower third, and vascular invasion, which seems to increase with the height of the lesion in the rectum.

No relation could be observed between the location of the lesions (anterior, posterior or lateral wall) and the presence of involvement of nerves. Sixteen (50.3 per cent) of the lesions in which nerves were involved were annular in type and the rest were located at different points on the rectal wall. In the entire series, 30 lesions (43 per cent) were annular.

TABLE V

RELATION OF PERINEURAL INVASION TO LOCAL RECURRENCES

	Nerves Involved		Nerves Uninvolved	
	Cases	Percentage	Cases	Percentage
Definite local recurrence	13	81.2	14	30.4
Definitely no local recurrence	3	18.8	32	69.6
Totals	16	100.0	46	100.0
Questionable and inadequate follow-up, and post-operative complications	14		24	
Grand Totals	30		70	

The striking feature of perineural involvement of rectal carcinoma is its relation to local recurrences (Table V). Only recurrences in the scar or site of anastomosis were considered. Metastasis to nearby viscera, such as the bladder, vagina, prostate, perineal nodes, etc., was eliminated because of the probability of its being due to lymphatic or venous spread rather than to invasion of nerves. Definite local recurrences were found in 81.2 per cent of traceable cases in which there was perineural invasion, whereas, in those without perineural invasion, recurrences occurred in only 30.4 per cent. Cases in which there were definitely no local recurrences comprised only 18.8 per cent of those in which nerves were involved, whereas, in cases

without involvement of nerves there were definitely no recurrences in 69.6 per cent. It was necessary to eliminate certain cases from each group in comparing these results. These were considered to have been followed-up inadequately because of early deaths from unrelated causes, such as post-operative peritonitis or pulmonary embolism, and unconfirmed causes of death. All cases in which there was a question as to local recurrence, but no reliable evidence was found to substantiate its presence, were placed in the latter group.

In the cases in which there was definite recurrence, there were nine (69.2 per cent) in which lymph nodes were involved in the group in which perineural invasion occurred, and there were seven (50 per cent) in which lymph nodes were involved in the group without perineural invasion. While these figures tend to indicate a somewhat greater degree of lymphatic spread in those cases of recurrence in which nerves are involved, they are not statistically significant, and, in any case, do not necessarily prove that recurrence is dependent on the lymphatic system rather than on the nerves. Nodal involvement in the entire series, in cases in which there was perineural involvement, was 66 per cent. Nodal involvement was 64.7 per cent (11 cases in 17) in those cases in which there was invasion of the nerves but no local recurrence.

There was a notable difference in the five-year survival rates of the patients who had, and those who did not have, perineural involvement. In the group of 29 traced cases in which there was perineural involvement, only two patients were living and well five years after the operation (6.9 per cent). Twenty-three were dead from cancer, either recurrent or metastatic, and of these, 19 were dead within two and one-half years. The average duration of life after operation of the 23 who died within five years, eliminating four patients who died because of postoperative complications, was 20 months.

In the group in which involvement of nerves was not found at operation, it was discovered that 18 of 51 patients who were traced, were living after five years (35.3 per cent). The average duration of life after operation in this group, of those who did not survive for five years was 25.7 months.

In the group in which there was perineural involvement, four patients, sooner or later, complained of a great deal of severe sciatic pain, which might be taken as a possible indication of further spread to greater distances, of the malignant cells within the perineural spaces. All four of these patients died within 15 months after operation of visceral metastatic lesions.

It has been mentioned earlier that perineural invasion can be traced for a considerable distance in some cases. Although measurements of this entire distance were not carried out in this study, perineural invasion did occur as far as four inches (10 cm.) from the site of the primary lesion. One might speculate that the invasion of the perineural spaces can take place to a distance above the line of operative resection and, at a later date, burst through the confines of the perineural space to give rise to a recurrent

lesion, perhaps at the line of anastamosis or at a higher level. Many sections showed a nerve surrounded by malignant cells. In these instances the perineural sheath appeared to be ruptured as though the cellular contents of the sheath had become too great for the distensibility of the membrane. In sections exhibiting 'secondary' nerve involvement, that is, isolation of a nerve by infiltrating carcinoma without penetration of the perineural membrane by the cells, the membrane was always intact, although completely surrounded by malignant cells.

Venous Invasion.—In 100 cases of rectal carcinoma studied in this series there was evidence of invasion of the veins in 20 cases. There may have been venous involvement in two others, but confirmation of its presence was impossible by the methods used.

The average age of the patients who had venous invasion was 47 years. The average duration of symptoms in cases in which there was invasion of the veins was 7.9 months. The duration of symptoms in these cases varied from three weeks to 30 months.

There were 13 men (65 per cent), and seven women (35 per cent) among the patients who had venous invasion.

The incidence of venous invasion in relation to histologic grading, according to cellular differentiation and to mural penetration (Tables II and IV) increased with the degree of malignancy. Only three of the 20 cases in which there was venous invasion fell into Dukes' Class B, while 17 cases fell into Class C. There were no cases in Class A.

Nodal involvement was present in all except three of the cases in which there was venous invasion (85 per cent). This would indicate that venous invasion rarely occurs before nodal involvement, but that it may do so.

In relating the frequency of venous invasion to the location of the lesion, we found that in lesions of the upper part of the rectum and rectosigmoid invasion was present more often than in lesions of the lower segments, the upper third in 55 per cent, and the middle and lower thirds in 15 and 30 per cent, respectively.

The postoperative survival of patients who had venous invasion was found to vary from four to 60 months, the average survival being 22 months. Three patients survived for three years, one patient for four years, and one for five years. The latter died exactly five years after operation, and, at necropsy, lesions were observed in the liver. Sixteen of the 20 patients finally succumbed to cancer.

In eight of these 20 cases venous invasion alone was observed, while in 12, perineural involvement was observed in addition to venous invasion. In 16 cases in the general series, involvement of nerves without venous invasion was observed.

In the total series of 100 cases, there were 27 local recurrences. In six of these, nerve invasion alone was observed (22.2 per cent); in three, venous involvement alone (11.1 per cent); in seven, involvement of nerves and veins together (25.9 per cent); and in 11, involvement of neither nerves

nor veins (40.7 per cent). In only four of the cases without involvement of nerves or veins was involvement of nodes observed. Therefore, in seven cases there was recurrence in spite of the fact that involvement of any of the three pathways of spread was not observed at operation.

Recurrence of rectal carcinoma, in the light of these findings, is probably not concerned with only one of the three pathways of spread, but results from different ones in different cases, and may involve any of them. However, it may be said that local recurrences are more frequent in rectal carcinoma when nerves and veins are involved than when they are uninvolved, and that there are twice as many recurrences when nerves alone are involved as when veins alone are involved.

In studying the relation of the three pathways of spread of rectal carcinoma to the presence of visceral metastatic lesions occurring at operation and later, it was found that metastatic lesions were present or occurred later most frequently in the group that showed venous invasion (Table VI).

TABLE VI

OCCURRENCE OF VISCERAL METASTATIC LESIONS AT OPERATION, AND LATER, IN CASES IN WHICH THERE WAS NODAL, PERINEURAL, OR VENOUS INVASION

	Entire Series		Nodal Involvement		Nerve Involvement		Vein Involvement	
	Cases	Percentage	Cases	Percentage	Cases	Percentage	Cases	Percentage
Metastatic lesions present at operation, or occurring later.....	31	45.6	22	78.6	13	81.2	16	94.1
Metastatic lesions.....	37	54.4	6	21.4	3	18.8	1	5.9
Totals.....	68	100.0	28	100.0	16	100.0	17	100.0
Inadequate follow-up, and postoperative complications.....	32		19		14		3	
Grand totals.....	100		47		30		20	

In 94 per cent of the cases in which venous invasion was observed at operation and in which the follow-up was adequate, visceral metastatic lesions either were present at the time of operation or developed later, whereas, visceral metastatic lesions were less frequent in cases in which nerves or nodes were invaded. This fact would seem to indicate that venous invasion is important in regard to visceral metastasis while perineural invasion may be related to local recurrence.

In the entire series of 100 cases, visceral metastatic lesions were found at the time of operation in seven cases, and in six of these, venous invasion was present in the specimen removed (86 per cent). Lymph nodes were involved in five of these seven cases (71 per cent).

In only four of the 20 cases in which there was venous invasion were metastatic lesions observed in the liver at operation, and the surgeon made the diagnosis of malignancy by palpation correctly in three instances.

When one considers that one-fifth of the patients in this series of rectal

carcinoma had veins invaded by carcinoma, and that practically all (94 per cent) of these already presented, or later acquired, visceral metastatic lesions, the prognostic importance of the presence of venous invasion in the operative specimen is seen. The fact that four-fifths of the patients in the series of 100 cases failed to show invasion of the veins at operation and that visceral metastatic lesions occurred in only 18.7 per cent (15) of these patients emphasizes the prognostic significance of the absence of venous invasion, as has been mentioned by Brown and Warren.[3]

CONCLUSIONS

1. In 100 cases of rectal carcinoma, lymph nodes were involved in 47 per cent, nerves in 30 per cent, and veins in 20 per cent.

2. Invasion of lymph nodes, nerves and veins increases with the degree of malignancy of the carcinoma.

3. Invasion of lymph nodes occurred equally in the two sexes, while venous invasion and perineural invasion were more frequent among men than among women.

4. Venous and nodal invasion occurred more often among young than among old patients, while invasion of nerves was not related to age.

5. Invasion of nerves was not related to the location of the lesion, while venous invasion was most frequent in lesions of the upper part of the rectum, and nodal invasion was slightly more frequent in lesions of the middle segment of the rectum than in lesions of other segments.

6. Venous invasion occurred more frequently in cases in which there was involvement of nodes than in other cases, but it occurred in cases without involvement of nodes as well.

7. Nodal invasion was somewhat more frequent in cases in which there was involvement of nerves than in those in which the nerves were not involved.

8. Pain was a prominent symptom in 89 per cent of cases in which there was invasion of nerves.

9. Local recurrence was more than two and one-half times as frequent in cases in which invasion of nerves was observed as in cases in which it was not observed.

10. Visceral metastatic lesions at operation, or later, occurred in 94 per cent of patients who had venous invasion in the primary growth, and were five times as frequent as in patients without venous invasion in the primary growth.

11. Venous invasion in the primary growth does not always mean that hepatic metastatic lesions are present.

12. Eighty-six per cent of patients among whom visceral metastatic lesions were present at operation exhibited venous invasion in the primary growth, while 71 per cent exhibited nodal invasion.

13. Eighty per cent of patients who had venous invasion in the primary growth died from carcinoma, either recurrent or metastatic.

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CHOLEDOCHUS CYST*

FINAL REPORT OF TWO CASES

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Case Report.—K. E., age 22, white, female, married, was admitted to the medical ward of the Chestnut Hill Hospital, September 9, 1940, and discharged September 18, 1940. She was readmitted for the same condition as a private patient of Dr. William C. Sheehan, now Lieutenant Colonel Sheehan, U. S. A., October 7, 1940, and discharged October 25, 1940. She was again readmitted to the service of Doctor Sheehan, October 16, 1941, and died October 22, 1941, of general peritonitis following rupture of a liver abscess.

Chief Complaint.—Pain and a tumor in the right upper abdomen and jaundice.

History of Present Illness.—Patient's symptoms were first noticed before her baby was born August 19, 1940. During the fourth and fifth months of her pregnancy there occurred occasional pains in the right upper quadrant of her abdomen. She described these pains as stomach pains since they were exaggerated when she ate. They were so severe and colicky in character that she was brought into the maternity ward and was given urinary antiseptics. Several months after the stomach pain, the pain shifted to the back and well up toward the shoulder, where it became constant, at first excruciating and then gradually decreasing in intensity until after one and one-half months, when the pain left her entirely, but the seventh month of her pregnancy she noticed a slight yellowish tinting of the skin, which came and went at irregular intervals and never became a real deep yellow. There also was an irregular diarrhea that continued almost until full term. Two weeks before the birth of the baby the mother looked very well, and there was no jaundice until 12 days after the baby was born. Then suddenly jaundice set in and increased in severity and remained constant. At this time a mass was noticeable in the right upper quadrant of the abdomen about the size of a grapefruit. This mass was noticed during the seventh and eighth months of pregnancy but had not been diagnosed as abnormal in any way, being taken for the fetus. There was no pain in this area for the last two months. *Past Medical History.*—Measles, catarrhal jaundice at age of 12. Influenza at five years of age. *Social History.*—Married, one child. *Family History.*—Irrelevant.

Physical Examination.—The patient was a white female, age 22; jaundiced. Frail build but muscular tone good. The positive findings were as follows: Skin: Jaundiced. No petechiae. Abdomen: Liver enlarged, palpable at least five fingers breadth below the costal margin. Gallbladder questionably enlarged, though apparently it seems as though there is a hydrops. Mass can be pushed downward with the palm of the hand obliterating everything except the liver edge. No herniae. *Laboratory Data:* Icteric index increased, van den Bergh 3.0 mg.% bilirubin; urine loaded with white cells. *Clinical Impression:* Hepatitis; hydrops of gallbladder.

Progress Notes.—One thousand cubic centimeters of 5% glucose in normal salt solution were given on September 10, 11, 12, 13, 15 and 16. September 18, 1940, discharged, and allowed to go home. If jaundice does not lessen in severity she is to be readmitted to the Surgical Service. Our Surgical Service was asked to see this patient in consultation during this admission but since the patient showed signs of lessened jaundice and decrease in the size of the mass she was allowed to go home.

* Read before the Philadelphia Academy of Surgery, December 7, 1942.

Second Admission.—Surgical Service of Dr. Sheehan: Admitted October 7, 1940. Discharged October 25, 1940. Patient was readmitted 19 days after discharge from the hospital, with persistent jaundice, and a tumor in the upper right quadrant equally as large as on previous admission, and the liver enlarged four fingers' breadth below the costal margin. After several days preoperative preparation the patient was scheduled for operation with the possible diagnosis of hydrops of the gallbladder.

Operation.—October 11, 1940 by Doctor Sheehan: Under nitrous oxide and oxygen anesthesia, the abdomen was opened. A large cystic mass was found under the right lobe of the liver with a gallbladder with its cystic duct resting on it and emptying into the cystic mass. A needle was inserted into the mass and bile-colored fluid obtained. A cholecystectomy and choledochoduodenostomy and appendicectomy were performed. About 1560 cc. of bile were removed from the cyst. Intravenous glucose 5% in 2000 cc. salt solution was given.

The patient was discharged October 25, 1940, after a rather stormy convalescence. The jaundice had gradually faded.

Third Admission to Chestnut Hill Hospital.—Admitted October 16, 1941, and died October 22, 1941. *History of Present Illness.*—Patient was in her usual health, having recovered from a choledochoduodenostomy on October 10, 1940, until October 12, 1941, when she experienced five or six chills, after which her temperature rose to 101° F. She had severe, drenching night sweats which required changing the bed every two hours. Loss of four or five pounds in the past three months. Usual weight 98 pounds. No cough. Had slight nausea with no vomiting. Appetite was good before onset of present symptoms.

Progress Notes.—October 18, 1941: Temperature 101° F. Feels flushed. W. B. C. 18,650 as compared with count on admission of 11,400. R. B. C. 3,000,000. Hemoglobin 61%. October 19, 1941: Chills and fever this P.M. Temperature 102.6° F. Pain in left upper abdomen radiating to lower abdomen. Also complains of chest pain. Abdomen somewhat distended. Chills frequent, spleen seems enlarged to percussion but is not palpable. Given intravenous glucose 5%, 1000 cc. October 20, 1941: W. B. C. 9,000, Polys. 78%. Given glucose 5% and salt, 1000 cc. Temperature, pulse and respirations fell to subnormal level this P.M. General condition worse. October 21, 1941: Given 500 cc. citrated blood. Barium enema today shows no evidence of a large bowel pathology; evidence of small intestinal obstruction. Blood chemistry: Chlorides 468; protein 6.7; CO_2 47; blood urea nitrogen 20. Temperature elevated this A.M., down this P.M. Pulse rate stays elevated. Distention much increased. Peristalsis not heard. Advised operation. Condition not good.

Operation.—October 22, 1941: Exploration revealed a massive pus collection in the abdomen and general peritonitis. Over three pints of creamy pus were aspirated. Appendix not located. Choledochal cyst found to be much decreased in size. Sulfanilamide powder was sprinkled into the abdominal cavity and several drains were inserted. Postoperative condition poor. Given fluids and blood transfusion and put in an oxygen tent, but condition became worse, and she expired shortly after operation was completed.

Autopsy Report. (Three hours after death). *Peritoneum and Gastro-intestinal Tract:* The entire peritoneum is involved in a diffuse and localizing inflammatory reaction. Every surface is covered by white fibrinous exudate which forms easily broken adhesions between the omentum, loops of bowel, body wall and all the intra-abdominal structures. In many locations these adhesions enclose similar or larger collections of thick creamy pus. Such collections are found everywhere but are more common in the upper parts of the abdomen. There are large deposits between the liver and the diaphragm. One such collection between the left lobe of the liver communicates with an irregular, ragged abscess cavity within the organ. The stomach contains a small

quantity of brownish fluid. Its structure is normal and its mucosa quite intact. The duodenum contains similar fluid and is equally normal. The ampulla of Vater projects from the surface and is easily identified. About 3 cm. proximal to it there is a small ostium which admits a grooved director easily and leads into a cystic structure described below. The remainder of the small and large bowel shows no lesions nor any point of weakness to suggest the possibility of leakage. There is no trace of an appendix.

Liver: Is normal in size, pale, rounded. The external surface is involved with the inflammatory process described. The viscus cuts easily. In the dependent portions of the left lobe there is a small, irregular, ragged abscess cavity described. This is about 6 cm. square and extends no further into the liver than 3 cm. Beneath the right lobe and projecting so, from the liver substance, as almost to seem a separate structure, is a cyst, approximately 9 cm. in diameter, with a thick, inflamed fibrous wall, into which liver tissue projects, filled with a thick greenish-yellow pus. Internally this is ragged and resembles an abscess.

Biliary Tract: The gallbladder has been removed and the gallbladder fossa is filled with scar tissue. The nature of the ampulla of Vater has been described. Proceeding upward from this structure is a small normal common duct about 15 mm. in length. From this point it dilated immediately into a cystic space, approximately 3 cm. in diameter and about 10 cm. in length, which extends into the sagital fossa of the liver. One side of it is attached to the duodenum and through this region runs the ostium described above. The cyst is not regular in shape but has four or five arms that project for a centimeter or two into the surrounding tissues. Several of these penetrate the liver and connect with the bile ducts in that organ. The cyst is lined by a thin, smooth, pale membrane and is filled with flakes of brown crystalline material that resembles crust. The same material is found in the larger intrahepatic bile duct in the neighborhood.

Pancreas: Is normal in size and shape. Its tissues are pale and show no abnormality. Wirsung's duct is easily patent for some distance above the ampulla of Vater.

Bacteriology: Culture of liver abscess and peritoneum reveal: 1. Streptococcic ignavus, nonhemolytic. 2. An unidentified enterobacterium probably belonging to the genus Proteus.

Pathologic Diagnosis: Heart—Apparently normal. Lungs—Bronchopneumonia. Spleen—Passive congestion. Kidney—Toxic nephrosis. Urinary tract—Apparently normal. Genitalia—Apparently normal. Peritoneum and Gastro-intestinal tract—Acute peritonitis, acute perihepatitis. Biliary tract—Choledochal cyst with choledochoduodenostomy. Pancreas—Acute peripancreatitis. Adrenal glands—Lipoid diminution. *Cause of Death:* Liver abscess with rupture and peritonitis.

COMMENT

A choledochus cyst (also reported as Congenital Cystic Dilatation of the Common Duct or Diverticulum of the Common Bile Duct) is interesting because of its pathology, diagnosis, treatment and complications or sequelae.

A true choledochal cyst represents a localized dilatation, primarily of the common duct, and the gallbladder is rarely enlarged.

The liver is frequently enlarged and cirrhotic. In a minority of cases the intrahepatic ducts are grossly dilated. Microscopically, there is often a cirrhosis with increased periportal connective tissue, proliferation of the bile capillaries, and rarely some bile stasis. Infection is common, and leukocytic infiltration of the portal areas may be marked. Cholangitis may reach an advanced stage, and intraductal suppuration has been seen.

DIAGNOSIS

It is a double satisfaction to diagnose these cases preoperatively and, again, at operation. Preoperatively, the diagnosis should be simple, since the outstanding three symptoms, namely, (1) pain in the right upper abdomen; (2) cystic tumor mass in the same area; and (3) jaundice, are the most likely to result as the lesion develops. However, the diagnosis is not often correctly stated. In a very complete article written by Zinninger and Cash,[1] in April, 1931, they state, "that the correct diagnosis before operation was apparently made three times in the 83 cases reported, and in many instances the true condition was not recognized at operation. Such errors will doubtless be repeated in the future, as few surgeons actually see a patient with this lesion. Therefore, unless the clinical picture is clear in the mind of the observer, it is unlikely that a correct preoperative diagnosis will be made."

TREATMENT

We have agreed that the treatment is choledochoduodenostomy. It is the simplest operation and the least shocking to the patient. Gross reports that in a group of 52 children originally collected and studied, the mortality was 69 per cent, but in those treated by primary anastomosis of the biliary tract and intestines, the mortality was nine per cent. Again, Ladd and Gross[2] definitely state that in many cases exploration has been continued unduly long, so that therapeutic procedures had to be curtailed because of onset of surgical shock. It is, therefore, pertinent to emphasize that, "the surgeon must be familiar with the pathology of this condition," for only then can he quickly recognize the lesion and rapidly promote drainage of the biliary system into the intestine, which has proved to be so efficacious in curing these individuals. Thus, even if the diagnosis is not made preoperatively, the probabilities of a cure are high if the condition is recognized at the operating table and proper treatment is immediately instituted.

In a number of cases the cyst has been drained externally in the hope of joining the ductal system and intestine at a later date. Such external drainage of the cyst has been followed by an exceedingly high mortality. Excision of the cyst should never be attempted. Doctor Weeder and the author originally thought in our case with a double duct and a cyst on the right one, that there was an advantage in excising it but we now agree that there is none. At the autopsy of Doctor Sheehan's case we found that the sac of the cyst had decidedly shrunk after a year's anastomosis (choledochoduodenostomy). This fact has many times been proven.

COMPLICATIONS OR SEQUELAE

In these two cases that I have seen and studied, the first case with Doctor Weeder,[3] the patient developed a cirrhosis of the liver after excision of the cyst from the right common duct. The second case, seen with Doctor Sheehan, developed a liver abscess and general peritonitis. The latter patient was well for a year after the choledochoduodenostomy, cholecystectomy

and appendicectomy, but then suddenly developed peritonitis, the result of a ruptured liver abscess, which resulted in her death.

There is a general impression that life expectancy is rather short after an internal biliary fistula has been established. This is largely due to the fact that in dogs an ascending infection through the bile passages occurs and death follows rather early. We may seriously question the truth of this observation as applied to man, if one reviews the statistics.

In our first case, in which cirrhosis of the liver developed, the boy was operated upon December 13, 1932. The child remained entirely well until January 1, 1936, when he complained of some generalized pain and distention of the abdomen. Two masses were palpable, with enlargement of the abdominal veins and also ascites. The laboratory reports showed a decided anemia, and a diagnosis of splenic anemia was made. A splenectomy was performed February 5, 1936. The child did fairly well except for variations in his blood counts until September 23, 1937, when he complained of great fatigue, nausea and vomited a large amount of bright red blood. He vomited blood again September 25, 1937, and was readmitted to the hospital; he improved definitely under treatment and was discharged November 11, 1937. After his discharge he steadily improved. There was no evidence of gastro-intestinal or other bleeding and his blood count in February, 1938, showed red cells 3,950,000, hemoglobin 63 per cent; white blood cells 10,100, polymorphocytes 48%, lymphocytes 37%, monocytes 12%, eosinophils 2%, and basophils 1%.

At the Joint Meeting of the Philadelphia Academy of Surgery and the New York Surgical Society at Philadelphia February 9, 1938, Doctor Weeder[4] reported the sequelae and complications of this case and, in conclusion, stated "certain questions are raised for which we have not the answer. It is interesting, however, to speculate upon them. Are these complications, the blood dyscrasia and the gastro-intestinal hemorrhage both the result of back pressure on the portal system, resulting from the atrophy of the right half of the liver and the fibrosis in the remaining part? Has the back pressure produced changes in the normal physiology of the spleen, resulting in alterations in function of the reticulo-endothelial system? If this be so, does Banti's disease originate in the liver, and is it the result of changes in that organ produced by toxins, either infectious, metabolic or disturbed endocrine secretions?"

In discussing Doctor Weeder's follow-up of this case, and in answer to the questions asked, Dr. Allen O. Whipple, of New York, gave a very interesting deduction and stated that: "The subsequent history of this case, with the development of a splenomegaly in the presence of a cirrhosis with portal-bed obstruction has greatly interested me. We have been greatly interested in our Combined Spleen Clinic, at the Presbyterian Hospital, in the pathogenesis of splenomegaly. In some patients, undoubtedly, intrahepatic portal obstruction results in a splenomegaly. In other cases, with thrombophlebitis of the splenic or portal vein proximal to the liver, spleno-

megaly developed without liver changes. In still others, portal-bed irritation, as seen in schistosomiasis and in dogs following silica powder injections of a portal radical, splenomegaly is associated with cirrhosis. In all of these several pathogeneses, the clinical picture is Banti's syndrome, *i.e.*, an anemia, a leukopenia, a low platelet count, and an enlarged spleen."

We are now interested to have the follow-up of all these cases that show a cirrhosis of the liver, in order to determine whether or not the cause is congenital or caused by interference at operation upon the choledochus cyst.

The child which Doctor Weeder and I operated upon December 13, 1932, was finally admitted to the Germantown Hospital, July 18, 1942, again suffering from gastro-intestinal hemorrhage from esophageal varices due to his portal obstruction, which finally resulted in his death July 23, 1942. At autopsy, a very pronounced cirrhosis of the liver was found with large esophageal varices. No other unusual ducts were found except the remaining common bile duct which was greatly contracted.

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ROUTINE CYSTIC DUCT DRAINAGE FOLLOWING CHOLECYSTECTOMY

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IT is not necessary to defend the statement that calculi are sometimes "left behind" in the common bile or hepatic bile ducts following operations upon the biliary tract. This is especially true when cholecystectomy only has been performed. However, the incidence is decreased if the biliary ductal system is thoroughly and systematically explored, and it varies in direct ratio to the experience of the operator and the methods used for exploration. Nevertheless, this unfortunate happening is always a possibility, and in some cases a probability. Because a remaining calculus in this location is ever a potentially serious, and even a fatal, complication, its consequences are worthy of prevention when and where possible. On the other hand, it is just as important to know that ductal calculi are absent as it is to know that they are present, particularly if a patient has symptoms following cholecystectomy. Hence a brief discussion of a simple, safe and very satisfactory method of determining these facts in every operative patient before they leave the hospital. The advantages of such knowledge are obvious.

The ideal procedure is a roentgenologic study of the common bile duct made on the operating table, using contrast media—but this is rarely done (the immediate cholangiogram). This procedure will undoubtedly be in more common use in the near future. It has, of course, certain disadvantages, but these are outweighed by its advantages. It not only decreases trauma and the operating time in the doubtful case by showing the absence of calculi, and that the duct need not, therefore, be opened, but if stones are present it shows accurately their number, size and position. Thus the immediate cholangiogram greatly reduces the incidence of secondary operations, with their higher morbidity and mortality rates. However, in those hospitals which have not the facilities for immediate cholangiography, such studies can be made at a later date on every patient—preferably before they leave the hospital—through a cystic duct drain introduced at the time of cholecystectomy. (Cholangiography is *always* a *must* procedure in all patients who have a mushroom catheter in the gallbladder or a tube in the common duct).

A small rubber catheter is placed in the remaining (proximal) cystic duct and securely tied with 40-day chromic catgut. If the diameter of the duct is small it may occasionally be necessary to cut the duct longitudinally before the catheter can be inserted, which was necessary in the case herein presented. The introduction of the tube takes only a few minutes longer than clamping and tieing the cystic duct stump because this entire area must be clearly

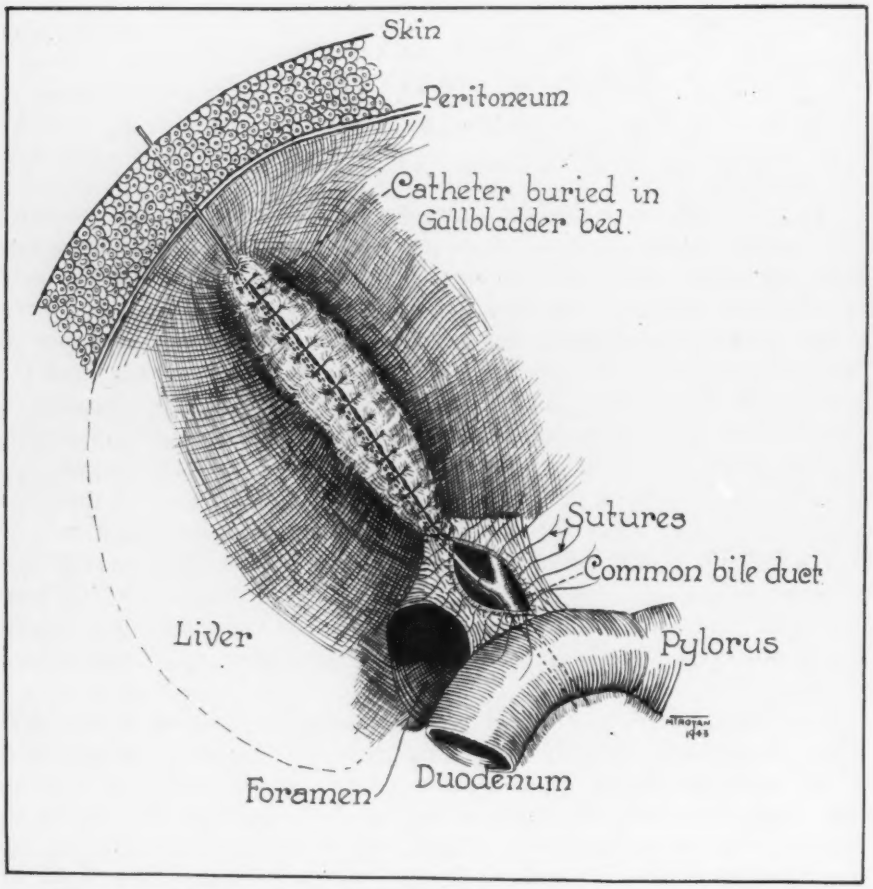

FIG. 1.—A semidiagrammatic drawing to illustrate the position of the catheter in the reperitonealized liver bed. The sutures will close the opening over the ductal juncture. Omental grafts should cover any defects in such a way that no bare areas remain.

visualized before the gallbladder is removed, whether or not the catheter is used. The catheter is then brought to the abdominal wall in the reperitonealized bladder bed (*i.e.*, under the peritoneum) and makes exit from the abdominal wall through a small stab wound immediately above the point where the catheter leaves the liver edge (Fig. 1). It may rarely be necessary to cover any bare areas with an omental graft; or a sleeve of omentum may have to be used to cover any length of rubber which is not retroperitoneal. In this way the foreign body is completely retroperitoneal except for a short distance between the liver and the abdominal wall. Adhesions are therefore minimized; nor does the cystic duct catheter produce excessive ductal secretion of mucus which may be a cause of symptoms following use of a T-tube. An example of the clinical value of routine cholangiography through a cystic duct drain is seen in Figure 2.*

* In those patients in which this procedure is not possible due to advanced disease and in which the common duct is not opened, the following is of value. (This will be

FIG. 2.—Female, age 28. Cholecystectomy. No apparent indications present to explore the common bile duct. Routine catheter drainage of cystic duct which was so small that it had to be "slit" before the catheter could be inserted. Cholangiograms made on the eighth day. Single cholesterol calculus clearly visualized; but only a very small portion of the supraduodenal portion of the duct is seen. The stone was removed before the patient was discharged from the hospital. Uninterrupted recovery. It can be well argued that such a large duct and such a large stone should have been discovered at operation, and, consequently, that it should have been removed. That is true, but the fact remains that it was not, and that this patient would have gone back to her life of hard housework with the law of averages very much in favor of her having a future and a serious illness. This undoubtedly occurs in a large proportion of cases but in this instance it was prevented by routine cystic duct drainage. The occurrence was embarrassing for the writer but it was also very fortunate for both the patient and the surgeon.

uncommon because if the disease is so extensive that the cystic duct cannot be intubated, the ductal system will almost invariably be involved and demand active interference). The duct is injected with dye (diodrast) immediately before the abdomen is closed and approximately 10–15 minutes after the administration of morphine gr.¼. (The advantages and disadvantages of the use of morphine to the closed sphincter of Oddi are now under consideration. Undoubtedly, in some instances, it influences the contour of the terminal duct and consequently the interpretation of the pictures.) The patient is then taken to the Roentgenologic Department on the way to their room from the operating theatre, and a cholangiogram is made. The roentgenogram is thus taken very soon after the injection of the dye. This is, of course, dependent upon the condition of the patient, the distance to the X-ray rooms, the temperature of the passage-ways through which the patient must pass, and other factors.

The cystic duct tube can also be used for prolonged drainage and perfusion. The writer is among those who consider these methods of value, because he believes that *cholecystopathy which needs surgical treatment cannot be present without involvement of the entire biliary system.* But the most important factor is the determination of the presence or absences of common duct calculi, either on the operating table or as soon after as possible.

Technic of Cholangiography.—Serial cholangiograms are necessary for correct clinical interpretations. Exposures are made after each injection of three cc. of 35% diodrast (17.5 per cent has been found quite satisfactory in thin patients). Usually four or five injections are sufficient to fill the duct. If the duct is very large injections of five or ten cubic centimeters are used. Two more exposures are made at approximately two and 10 minutes after the inhalation of amyl nitrite. By this method roentgenograms are taken during the filling and emptying phases. Thus, negative or positive shadows are more easily detected, and the constancy of their contour more definitely known. The latter is important in ruling out artefacts. All exposures before the duct is emptied should be made with the patient in the Trendelenberg position. In this way the liver radicals will fill more easily and the dye will not leave the duct until it overflows. Complete filling is, therefore, more likely. The evacuation roentgenograms (the emptying phase) are made in a partial Fowler's position.

CONCLUSIONS

Routine insertion of a small catheter into the cystic duct stump following cholecystectomy, for the purpose of performing cholangiography, is advocated. Thus, it can always be determined, in every patient, whether or not calculli remain in the common duct. The disadvantages of the procedure, to both patient and surgeon, are minimum; the advantages are maximum. The catheter also serves other purposes, for example, drainage; perfusion, if, and when, necessary; and possible dissolution or fragmentation of a calculus if one is found.

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INTESTINAL OBSTRUCTION DUE TO A GALLSTONE

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THIS REPORT of intestinal obstruction by gallbladder calculi is presented because of the clarity of roentgenologic demonstration and to add another verified case to the literature. Of the 36 cases previously recorded in which roentgenologic examination was made prior to operation, 22 revealed visualization of the biliary radicles. Although this sign was present on all the preoperative films, it was not recognized until after correlation with the operative findings.

Whenever gallstones have perforated through the gallbladder into the intestinal tract, there is usually a stoma sufficiently large to permit the reflux of intestinal or stomach contents into the gallbladder and biliary ducts. Since a barium meal is usually contraindicated in intestinal obstruction, the most common roentgenographic sign is the presence of gas in the gallbladder or hepatic system.

The following signs have been recognized roentgenologically:

1. Air or contrast medium in the biliary tract.
2. Complete or partial intestinal obstruction, as noted by distended loops of bowel.
3. Visualization of the stone by a plain film, or by the ingestion of a barium meal, permitting the outlining of a radiolucent calculus.
4. Change in position of a previously observed stone.

Case Report.—Hosp. No. 9467: M. H., white, female, age 55, married, was admitted to the Memorial Hospital of Queens, Jamaica, N. Y., April 13, 1942, with a history of upper abdominal pain and vomiting of six days' duration. The abdominal pain was constant, with intermittent exacerbations, and vomiting had become increasingly severe. The patient's health for the past few years had been generally poor, and she had been under treatment for hypertension, thyrotoxicosis, anorexia, and constipation, on various occasions. She had had a rather severe episode of abdominal pain and vomiting about ten years ago.

Physical Examination.—The patient appeared critically ill, dehydrated, apparently in acute pain, and was vomiting dark brown material at frequent intervals. The abdomen was generally distended, tympanitic, with a few distant borborygmi on auscultation. There was marked tenderness, with rebound pain, throughout the upper abdomen, but no evidence of rigidity or palpable masses. Temperature 97.2° F., pulse 140, B. P. 140/100, respirations 30. R. B. C. 5,700,000; Hb. 112%; W. B. C. 11,250, with 81% polys. Blood sugar—200 mg.; N. P. N.—360, chlorides—300, Urine—1+ albumin, 4+ sugar, negative acetone, 2+ indican, and numerous granular casts.

* Captain, M. C., U. S. Army.

Immediate replacement therapy of fluids, proteins, chlorides, and vitamines was started intravenously. Gastro-intestinal intubation was instituted, with continuous suction. An initial plain film of the abdomen was taken, followed by the administration of a small amount of thin barium mixture through the tube, and serial roentgenograms were taken. After the roentgenologic examination the barium mixture was recovered by aspiration through the tube.

The patient's general condition improved under supportive therapy and, on April 16, 1942, celiotomy was performed through a right rectus incision. Exploration

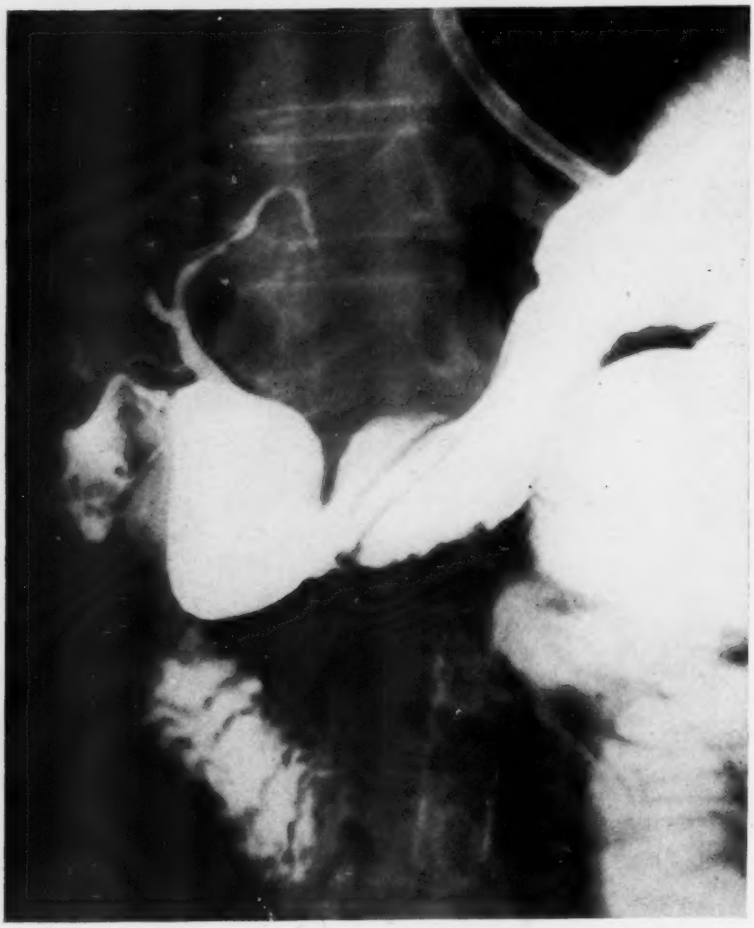

FIG. 1.—Roentgenogram showing stomach filled with barium, and the cholecystoduodenal fistula. The gallbladder is outlined by calculi, and the biliary radicles are delineated by the barium reflux.

revealed a round, obstructing calculus, the size of a large walnut, impacted, apparently, in the lower ileum. The proximal small intestine was markedly distended, atonic, but of good color. The ileum was incised longitudinally, and the obstructing calculus removed. The intestine was closed transversely, without diminution in the size of the lumen. There was almost immediate restoration of peristalsis in the distal bowel. Sulfanilamide was powdered about the site of the intestinal repair and into the general peritoneal cavity. The abdomen was closed without drainage.

The patient's postoperative convalescence was uneventful with the exception of

the passage of 14 faceted calculi per rectum during the 48 hours postoperative. The patient was discharged May 10, 1942, and has remained completely well to date.

Roentgenologic Report.—The stomach revealed no intrinsic pathology. The duodenal cap was markedly dilated and the barium flowed into a small sac (the gallbladder), and then into the cystic duct and the hepatic radicles. The gallbladder was

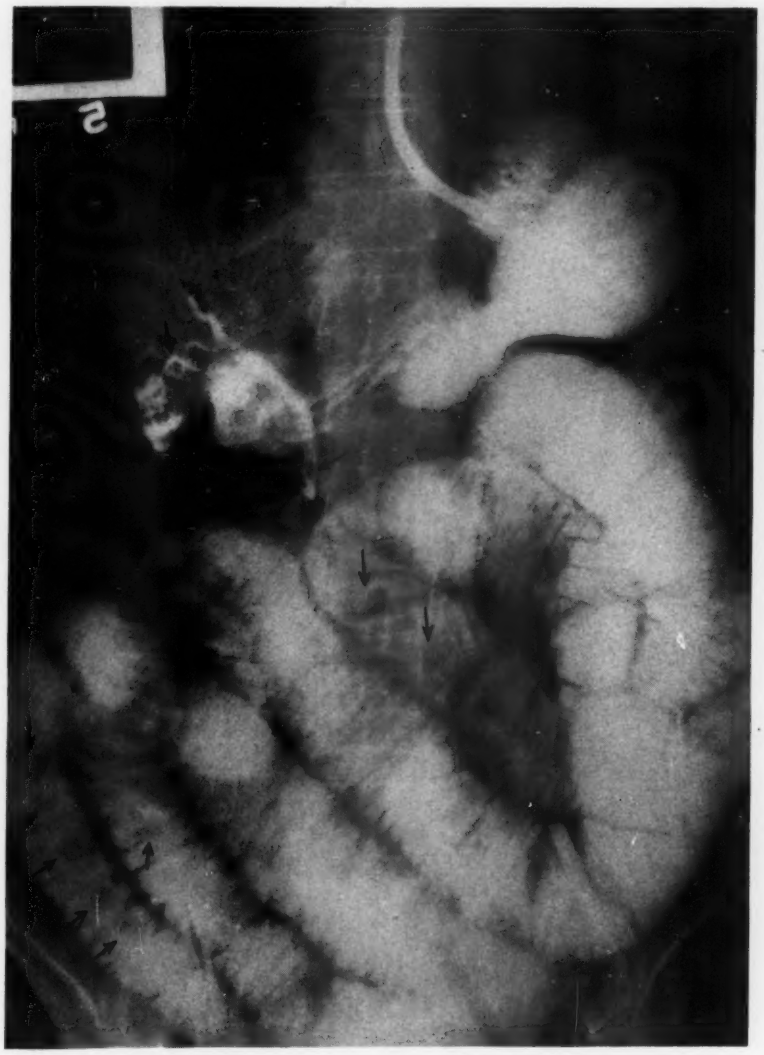

FIG. 2.—Roentgenogram (five-hour film) showing the great dilatation of the jejenum with the contained multiple, faceted, radiolucent calculi (arrows). The cholecystoduodenal fistula is clearly outlined as well as the stones in the gallbladder and the one in the common duct just proximal to the sphincter of Oddi.

firmly attached to the first part of the duodenum, and contained several radiolucent faceted shadows, significant of calculi. The upper small bowel was greatly dilated (Fig. 1).

After five hours there was considerable gastric and duodenal retention of the barium. The gallbladder and ductal system, including two intrahepatic radicles, were clearly visualized as well. An oval, radiolucent stone could be demonstrated in the common

duct just proximal to the sphincter of Oddi. Above this, the common duct was dilated. The jejenum appeared three to four times its normal size, and contained approximately 11 faceted, radiolucent stones (Fig. 2).

A 24-hour study revealed considerable gastric retention, and the remaining barium meal had progressed only slightly, and was still present in the upper small bowel. A

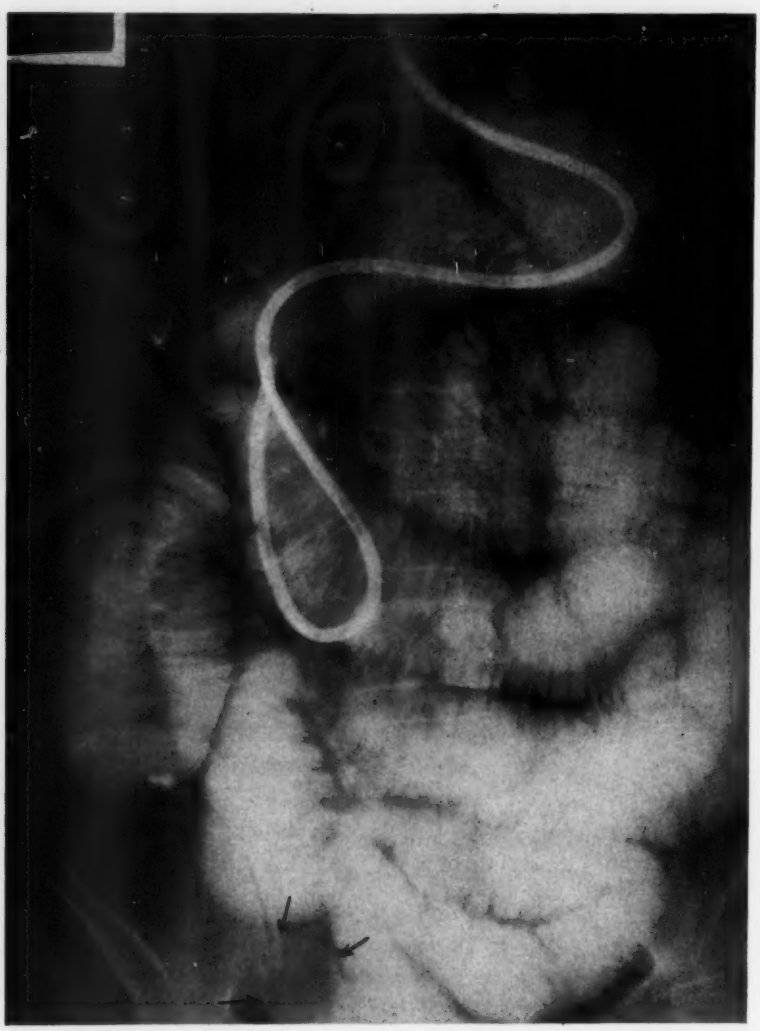

FIG. 3.—Roentgenogram (24-hour film) showing the distension of the proximal, small bowel; and the large calculus producing obstruction near the junction of the ileum and jejenum (arrows).

definite communication between the gallbladder and the duodenal cap was visualized at this time. In the right lower quadrant a large, oval, circumscribed shadow of decreased density, surrounded by a calcified rim of increased density was present. Proximal to this apparent calculus the small intestines were markedly distended and contained the numerous other calculi (Fig. 3).

After a period of 30 hours, there had been no progress of the barium meal, indicating, apparently, a complete obstruction at a level of the proximal ileum. The large

calculus did not appear to have changed its position in comparison with the previous study (Fig. 4).

At operation, the large calculus which produced the obstruction was removed. Figure 5 shows the calculus removed, surrounded by 15 faceted stones, which were passed per rectum.

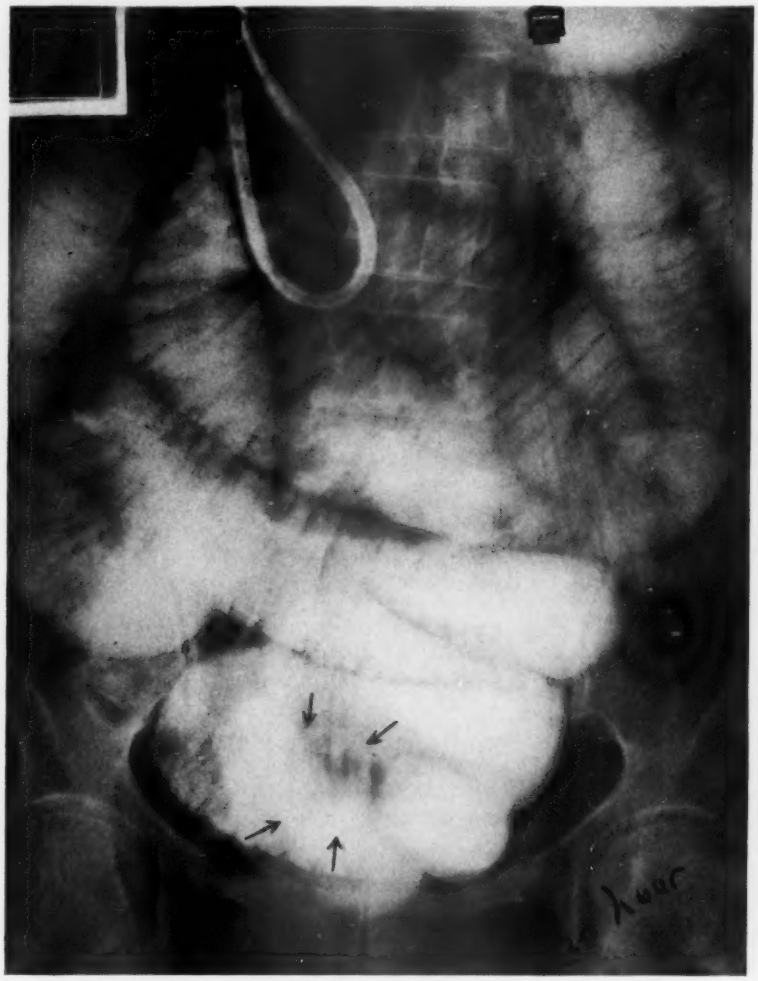

FIG. 4.—Roentgenogram (30-hour film) showing the large calculus again visualized, with its outer, calcified ring (arrows).

SUMMARY

This report of an instance of intestinal obstruction due to gallstones, resulting from a cholecystoduodenal fistula, illustrated the value of an early diagnosis, determined roentgenologically. With the proper technic, and serial observations, it is possible, in many instances, to localize the exact point of obstruction for the surgeon. Furthermore, the utilization of intestinal intubation contributed materially to the management of this case:

(1) By enabling decompression of the intestinal tract preliminary to

definitive operative treatment of the obstruction; and (2) by permitting the administration of a small, thin barium mixture for roentgenographic identification of the nature and location of the obstructing agent, followed by the safe, easy removal of the barium mixture through the tube.

FIG. 5.—Photograph, in the center of which is the large calculus removed at operation, which produced the obstruction and which is surrounded by the smaller faceted calculi which were passed per rectum following operation.

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RESULTS OF GALLBLADDER SURGERY IN DIABETES MELLITUS

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SEVENTY-SIX diabetic patients have had gallbladder surgery in this clinic during the 16 years from 1926 through 1941. The incidence of gallbladder disease in the diabetic has been reported in several large series and no attempt will be made here to extend these data. On the other hand, little information has been formulated about the results of gallbladder surgery in the patient with diabetes. Because information about these 76 patients, both preoperatively and follow-up, is almost entirely complete, these data may be found valuable to the physician who advises operative treatment of gallbladder disease in the patient with diabetes, particularly in consideration of the question of (1) any greater operative risk; (2) of the effect that the operation may have upon the diabetes; and (3) of whether or not diabetes will tend to favor the persistence of biliary tract infection that would in a normal person subside.

The problem of adequate nutrition and dietary regulation for the diabetic, already somewhat of a task for both physician and patient, meets a substantial *impasse* with recurrent episodes of biliary colic and gastro-intestinal upsets, and it is the sick, bewildered patient, frequently in hypoglycemia or acidosis, who waits for spontaneous relief but finally comes into the hospital for surgery.

Dr. Leland S. McKittrick performed the operations upon all the patients in this series except two. By virtue of a single operator, the error inherent in variation of approach and technic is avoided. The medical management has been in the hands of members of this clinic.

Classification of this series is made under the headings cholecystitis, cholelithiasis, choledocholithiasis, cholelithiasis with complications, infectious cirrhosis of the liver, and neoplasms of the gallbladder or pancreas. In Table I are the compiled data of the 76 diabetic patients who have had gallbladder surgery prior to January, 1942. Sixty-five are benign gallbladder disease, one is infectious cirrhosis of the liver, two are carcinoma of the gallbladder, and eight are carcinoma of the pancreas.

Analysis of the data in Table I show that 83 per cent of those coming to operation are women; the average age at operation is 58 years. The duration of diabetes before operation is from one month to 25 years for primary gallbladder disease, excluding carcinoma; the average duration of diabetes before operation is five years. The youngest patient is age 14. Two were operated upon at the age of 79; one of these (Case 40) is a man

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who had diabetes for 23 years prior to the development of gallbladder symptoms, and he came to operation complaining of pain, nausea, vomiting and jaundice. A cholecystectomy and choledochostomy were performed; he had an uneventful recovery, there was never recurrence of his symptoms, and four years later he died at the age of 83 with pulmonary tuberculosis. The other patient (Case 45) who was operated at age 79 had symptoms of gallbladder disease which developed at age 71, concomitant with his diabetes; a cholecystectomy and choledochostomy were performed, and three years later, in January, 1942, at the age of 82, he was alive and asymptomatic.

Empyema, gangrene, hydrops of the gallbladder, biliary tract perforation and pancreatitis are included as complications of benign gallbladder disease. There are 14 patients (22 per cent) in this series who came to operation with such complications. Hydrops of the gallbladder appeared three times, empyema twice, empyema and gangrene of the gallbladder once, partial or free perforation of the biliary tract nine times. The operative mortality for the entire series is in this group of patients with gallbladder disease and its complications, except for one patient (Case 36), a 77-year-old man with common duct stones. Apart from the immediate mortality (14 per cent), the results in patients with complications are 100 per cent good for permanent relief of symptoms (one patient is exempt because follow-up information was not obtained at the time of writing this paper).

Perforation of the biliary system by calculi occurred in nine of 65 patients coming to operation without neoplasm, or 14 per cent. Five of the nine were partial perforations, four were free perforations. Three of the perforations were in acutely inflamed gallbladders. Three were in gallbladders with emypema. This relatively high incidence is in agreement with the well known fact that the diabetic patient cannot limit infection normally. Commonly quoted statistics in all biliary tract disease are one to three per cent perforation, in contrast to the 14 per cent in this series. Eliason and McLaughlin[8] quote, without mention of the presence or absence of diabetes, the incidence of perforation as 0.9 per cent to 2.5 per cent in 6,816 cases reported by five authors. In 775 gallbladder cases of Eliason and McLaughlin there were 17 (two per cent) who perforated; one of these had diabetes. Heuer[9] reports an incidence of 26 per cent perforation in acute cholecystitis in nondiabetic patients.

Operative mortality for the entire group is 3.9 per cent; for those with benign gallbladder disease alone it is 4.6 per cent; this includes acute and chronic cases and those with complications. McKittrick[1] has recently reported data on all his surgery in both diabetic and nondiabetic patients with nonmalignant gallbladder disease. The majority of these were operated upon at hospitals other than the New England Deaconess Hospital. Operative mortality in these cases was 6.2 per cent for 81 diabetic patients, and 3.1 per cent for 286 patients without diabetes. Rabinowitch[2] reports an operative mortality of four per cent in 50 diabetic patients with chronic gallbladder disease.

The results of operative treatment of nonneoplastic gallbladder disease in the diabetic patients reported in this series compare favorably with those in the nondiabetic. Complete relief of symptoms was obtained in 77 per cent, partial relief in 12 per cent, and no relief in 11 per cent. Those who were alive in January, 1942, had survived operation from one to 14 years, an average of five and one-half years, and, in 1942, their average age is 63 years. Those who survived operation but who were dead in January, 1942, from any cause, lived an average of six years after operation, and died at an average age of 70. Fowler[3] reported, in 1933, the end-results in the operative treatment of 979 cases of gallbladder disease in nondiabetics; complete relief of symptoms was afforded in 81.8 per cent, partial relief in 10.5 per cent, and no relief in 7.7 per cent.

Of the 13 operative failures, nine, or 70 per cent, had demonstrable gallbladder stones and concomitant cardiac, psychoneurotic, or gastric symptoms; subsequent to operation, it is now conservatively estimated, that in six of these nine failures the primary complaint was extrabiliary in origin. Prognosis must be guarded for operative treatment in the diabetic who shows evidence indicating coronary heart disease. Five of the 13 failures in this series had arteriosclerotic or hypertensive heart disease which, in the light of subsequent findings on follow-up examinations, was clearly the chief source of the patients' complaints. Root, Bland, Gordon and White[4] have shown that coronary occlusion in diabetics over age 50 is three to eight times that in the nondiabetic. With this in mind, one must pay particular attention to the cardiac status of the diabetic patient, and attempt to make proper evaluation of both the biliary and cardiac systems for determination of that part which each may contribute to the patient's symptoms. McKittrick[5] states that he can see "no indication for surgery in the so-called cholecystitis without stones. Only once or twice in a surgeon's career does he see, at operation, true infection of the gallbladder in the absence of stones. Results following cholecystectomy in nondiabetic patients for so-called cholecystitis without stones are too uncertain to justify this procedure in the diabetic patient."

This study does not bear out the postulate that eradication of a diseased gallbladder will either heal or lessen the severity of the diabetes, as measured by the insulin requirement one year before and one year after operation, provided all else remains as constant as possible in the life's habits of this clinic's diabetic patients. Considering 56 patients who had benign gallbladder disease with calculi, and who are suitable for comparison, the average insulin requirement one year before operation, when it is likely that the stones and associated bladder changes were present, was precisely the same as that one year after operation, namely, 21 units.

One unusual case has been excluded from the averages because the degree of insulin resistance was so great during the period prior to operation, and immediately thereafter, that her case stands apart from the rest of the series and, therefore, has not been included in the averages. This

TABLE I

RESULTS OF GALLBLADDER SURGERY IN DIABETES MELLITUS

Case	Sex	Diagnosis	Operation	Age at Oper.	Alive or Dead	Duration of Diabetes, 1942 Yrs.	Duration of Diabetes before Gb. Symptoms Yrs.	SYMPTOMS Before Operation: Pain	Indigestion	Jaundice	SYMPTOMS After Operation: Pain	Indigestion	Jaundice	INSULIN REQUIREMENT One Year: Before Oper.	After Oper.
1	F	Cholecystitis	Cholecystectomy	70	d@	71	3	2	+	+	0	+	+	0	..	..
2	F	Cholelithiasis	Cholecystectomy	42	a@	56	18	4	+	+	0	Occ.‡	0	0	15	15
3	F	Cholelithiasis	Cholecystectomy	43	a@	57	16	1	+	+	0	0	0	0	20	20
4	F	Cholelithiasis	Cholecystectomy	65	d@	74	12	3	+	+	0	0	0	0	12	12
5	M	Cholelithiasis	Cholecystectomy	42	a@	53	18	0	+	+	0	0	0	0	0	0
6	F	Cholelithiasis	Cholecystectomy	68	a@	70	22	indef.	0	0	0	0	0	0	42	38
7	F	Cholelithiasis	Cholecystectomy	44	a@	58	21	7	+	+	0	0	0	0	0	0
8	F	Cholelithiasis	Cholecystectomy	60	a@	73	25	1	+	+	0	0	0	0	24	24
9	F	Cholelithiasis	Cholecystectomy	51	d@	55	9	0	+	+	0	?	?	?	20	?
10	F	Cholelithiasis	Cholecystectomy	63	d@	68	19	6	+	0	0	0	0	0	..	26
11	F	Cholelithiasis	Cholecystectomy	43	d@	50	9	2	+	+	0	0	0	0	0	0
12	F	Cholelithiasis	Cholecystectomy	42	a@	52	12	0	+	+	0	0	0	0	20	42
13	F	Cholelithiasis	Cholecystectomy	57	a@	69	17	2	+	+	0	0	0	0	40	40
14	F	Cholelithiasis	Cholecystectomy	53	a@	63	10	0	+	+	0	0	0	0	18	10
15	F	Cholelithiasis	Cholecystectomy	52	a@	54	17	15	+	+	0	0	0	0	25	28
16	F	Cholelithiasis	Cholecystectomy	56	a@	61	9	2	+	+	0	0	0	0	52	42
17	F	Cholelithiasis	Cholecystectomy	49	a@	52	8	5	+	+	0	0	0	0	0	0
18	F	Cholelithiasis	Cholecystectomy	48	a@	50	13	10	+	+	0	0	Occ.	0	25	55
19	F	Cholelithiasis	Cholecystectomy	49	a@	57	9	0	+	+	0	0	0	0	28	8
20	F	Cholelithiasis	Cholecystectomy	60	a@	66	6	indef.	+	+	.0	0	0	0	16	12
21	F	Cholelithiasis	Cholecystectomy	52	a@	54	9	7	+	+	0	0	0	0	38	38
22	F	Cholelithiasis	Cholecystectomy	62	a@	62	9	8	+	+	0	0	0	0	0	0
23	F	Cholelithiasis	Cholecystectomy	74	d@	84	16	6	+	0	0	+	0	0	5	5
24	F	Cholelithiasis	Cholecystectomy	32	a@	37	13	indef.	0	+	0	0	+	0	10	12
25	F	Cholelithiasis	Cholecystectomy	14	a@	25	12	0	+	0	0	+	0	0	26	38
26	F	Cholelithiasis	Cholecystectomy	56	a@	65	10	0	+	+	0	0	+	0	5	5
27	F	Cholelithiasis	Cholecystectomy	63	d@	65	14	5	+	+	0	+	+	0	5	5
28	F	Cholelithiasis	Cholecystectomy	63	a@	67	15	0	+	0	0	+	+	0	20	6
29	F	Cholelithiasis	Cholecystectomy	62	a@	67	5	2 mos.	+	+	0	+	+	0	12	12
30	F	Cholelithiasis	Cholecystectomy	58	a@	63	12	6	+	+	0	+	+	0	12	12
31	F	Cholelithiasis	Cholecystosomy	66	a@	70	5	0	+	+	0	0	0	0	12	0
32	F	Cholelithiasis	Cholecystosomy	71	a@	72	23	1 mo.	+	+	0	0	0	0	56	56
33	M	Cholelithiasis	Cholecystectomy and Choledochostomy	65	a@	68	29	25	+	+	+	+	+	0	26	42
34	F*	Cholelithiasis	Cholecystectomy and Choledochostomy	56	d@	65	15	5	+	+	+	0	0	0	20	15
35	F	Cholelithiasis	Cholecystectomy and Choledochostomy	43	a@	45	9	6	+	+	0	+	0	0	40	42
36	M	Choledocholith.	Choledochostomy	71	d@	72	7	4	+	+	+	0	0	0	12	12
37	F	Choledocholith.	Choledochostomy	77	died postop.		1	0	0	+	+	—	—	—	0	—
38	F	Choledocholith.	Cholecystostomy and Choledochostomy	69	a@	71	2	0	0	+	+	0	0	0	30	0
39	F	Cholelithiasis and Choledocholith.	Cholecystectomy and Choledochostomy	60	a@	67	32	25	+	+	+	0	0	0	30	40
40	M	Cholelithiasis and Choledocholith.	Cholecystectomy and Choledochostomy	79	d@	83	27	23	+	+	+	0	0	0	0	14

‡ *Glossary:* "Occ."= occasional, and not significant to the patient.

* Operated upon by Dr. D. F. Jones.

TABLE I—(*Continued*)

RESULTS OF GALLBLADDER SURGERY IN DIABETES MELLITUS

Case	Sex	Diagnosis	Operation	Age at Oper.	Alive or Dead	Duration of Diabetes, 1942 Yrs.	Duration of Diabetes before Gb. Symptoms Yrs.	SYMPTOMS Before Operation: Pain	Before Operation: Indigestion	Before Operation: Jaundice	After Operation: Pain	After Operation: Indigestion	After Operation: Jaundice	INSULIN REQUIREMENT One Year: Before Oper.	INSULIN REQUIREMENT One Year: After Oper.
41	F†	Cholelithiasis and Choledocholith.	Cholecystectomy and Choledochostomy	61	d@	71 17	0	+	+	0	+	+	0	10	10
42	M	Cholelithiasis and Choledocholith.	Cholecystectomy and Choledochostomy	47	a@	56 13	0	+	+	0	0	0	0	0	0
43	F	Cholelithiasis and Choledocholith.	Cholecystectomy and Choledochostomy	71	d@	80 12	1	+	0	+	0	0	0	0	0
44	F	Cholelithiasis and Choledocholith.	Cholecystectomy and Choledochostomy	64	a@	76 18	0	+	+	+	0	0	0	20	40
45	M	Cholelithiasis and Choledocholith.	Cholecystectomy and Choledochostomy	79	a@	82 11	1 mo.	+	+	0	0	0	0	0	0
46	F	Cholelithiasis and Choledocholith.	Cholecystectomy and Choledochostomy	49	a@	52 4	2	+	+	0	0	0	0	8	8
47	F	Cholelithiasis and Choledocholith	Cholecystectomy and Choledochostomy	63	a@	65 18	2	+	+	+	0	0	0	10	10
48	F	Cholelithiasis and Choledocholith	Cholecystectomy and Choledochostomy	57	a@	59 5	0	+	+	+	0	0	0	0	0
49	M	Cholelithiasis and Choledocholith	Cholecystectomy and Choledochostomy	37	a@	40 12	1	+	+	0	+	+	0	67	120
50	F	Cholelithiasis and Choledocholith	Cholecystostomy and Choledochostomy	84	a@	87 19	14	+	+	+	0	0	0	0	0
51	F	Cholelithiasis and Choledocholith	Cholecystostomy and Choledochostomy	52	a@	57 8	4 mos.	0	+	+	0	0	0	24	12
52	F	Cholelithiasis Hydrops of Gb.	Cholecystectomy	54	died postop.	8	1	+	+	0	—	—	—	24	—
53	F	Cholelithiasis Hydrops of Gb.	Cholecystectomy	52	a@	53 10	9	+	+	0	0	0	0	60	48
54	F	Cholelithiasis Hydrops of Gb.	Cholecystectomy	44	a@	47 7	1	+	+	0	0	0	0	40	50
55	F	Ac. Cholecystitis and Cholelithiasis, with partial perforation of Gb.	Cholecystostomy	68	d@	70 20	5	+	+	0	0	0	0	24	24
56	F	Ac. Cholecystitis and Cholelithiasis, with perforation	Cholecystectomy and Choledochostomy	58	a@	58 9	indef.	+	+	0	0	0	0	16	8
57	F	Cholelithiasis, with partial perforation	Cholecystectomy	57	a@	59 9	7	+	+	0	0	0	0	56	20
58	M	Cholelithiasis, with gangrene of Gb. & partial perforation	Cholecystostomy	63	d@	68 25	20	+	+	0	0	0	0	0	0
59	M	Cholelithiasis, empyema, & partial perforated Gb.	Cholecystectomy	55	died postop.	13	13	+	+	0	0	0	0	0	16

† Operated upon by Dr. Frank H. Lahey.

TABLE I—(*Continued*)

RESULTS OF GALLBLADDER SURGERY IN DIABETES MELLITUS

Case	Sex	Diagnosis	Operation	Age at Oper.	Alive or Dead	Duration of Diabetes, 1942 Yrs.	Duration of Diabetes before Gb. Symptoms Yrs.	SYMPTOMS Before Operation: Pain	Indigestion	Jaundice	SYMPTOMS After Operation: Pain	Indigestion	Jaundice	INSULIN REQUIREMENT One Year: Before Oper.	After Oper.
60	F	Cholelithiasis, empyema & gangrene of Gb., with perforation	Cholecystostomy	58	a@	63	21 9	+	+	0	0	0	0	24	24
61	F	Cholelithiasis, empyema, & partial perforation Gb.	Cholecystostomy	78	a@	84	7 1	+	+	+	0	0	0	0	0
62	F	Cholelithiasis with perfor. & abscess	Choledochostomy	61	d@	69	12 indef.	+	0	0	0	0	0	0	0
63	M	Ac. Cholelithiasis, choledocholithiasis, with perforation	Cholecystectomy and Choledochostomy	69	d@	72	5 2	0	+	+	0 (for two years)	0	0	18	12
64	F	Cholelithiasis and sub. ac. pancreatitis	Cholecystectomy and Choledochotomy	73	d@	73	18 0	+	+	+	?	?	?	15	—
65	F	Cholelithiasis and sub. ac. pancreatitis	Cholecystectomy and Choledochotomy	56	a@	63	23 16	+	+	0	0	0	0	22	22
66	M	Cirrhosis of liver, infectious	Cholecystogastrostomy	52	a@	65	16 indef.	0	+	+	0	0	0	0	0
							NEOPLASTIC							Duration Postoper. until Return of Symptoms	
67	F	Carcinoma of Gb. & cholelithiasis	Cholecystectomy and Choledochostomy	55	d@	58	4 3 mos.	+	+	+	20 mos.	0	20 mos.	0	0
68	M	Carcinoma of Gb. and cholelithiasis	Cholecystostomy and Choledochostomy	66	a@	69	3 0	0	+	+	0	0	31 mos.	12	16
69	F	Carcinoma of pancreas and cholelithiasis	Cholecystostomy	52	d@	53	7 mos. 1 mo.	+	+	+	+ Died 7 mos. after onset symptoms	+	? Died 11 mos. after onset symptoms	42	?
70	F	Carcinoma of pancreas and cholelithiasis	Cholecystogastrostomy	68	d@	69	2 9 mos.	0	+	+	6 mos.	7 mos.	8 mos.	30	18
71	F	Cholelithiasis, with ? carcinoma of pancreas	Cholecystostomy and Choledochostomy	69	a@	69	1 1	0	0	+	0 Postoperation—6 mos.	0	0 Died 5 mos. after onset symptoms	28	20
72	F	Carcinoma of pancreas	Cholecystogastrostostomy	64	d@	65	1 8 mos.	0	+	+	?	?	0 Died 24 mos. after onset symptoms	—	—
73	F	Carcinoma of pancreas	Choledochoduodenostomy	45	d@	47	30 mos. 8 mos.	+	0	+	10 mos.	?	16 mos.	25	16
74	F	Carcinoma of pancreas	Choledochoduodenostomy	58	d@	58	2 1	+	+	+	3 mos.	3 mos.	5 mos. Died 9 mos. after onset symptoms	15	?
75	M	Carcinoma of pancreas	Cholecystogastrostomy	67	d@	68	10 mos. 4 mos.	+	+	+	?	?	? Postoperation—8 mos.	15	?
76	F	Carcinoma of pancreas	Cholecystogastrostomy	70	a@	71	1 6 mos.	0	0	+	0	0	0	—	—

patient, a woman of 64 years (Hosp. No. 19110), developed insulin resistance during the five months preceding operation for common duct stones, when she had jaundice constantly, such that she required 300 to 400 units of insulin a day before operation and actually required 1000 units of insulin each day during a brief period following operation. However, during the next month, the insulin requirement rapidly declined, and two years after operation she was sugar-free, with normal blood sugars, without any insulin whatsoever. Although we cannot dismiss the influence of chronic jaundice and obstruction by stones in the common duct in producing this extraordinary degree of insulin resistance, the exact relation between the jaundice and the insulin resistance is not entirely clear.

The question has often been raised whether patients who suffer jaundice either because of toxic damage to the liver or infectious hepatitis are likely later to develop diabetes. In clinical experience it is sometimes difficult to relate jaundice to diabetes, especially since cases of cirrhosis of the liver with jaundice not uncommonly show a remission of the diabetes. Glucose tolerance curves will often show curious divergences during jaundice, some being low and some showing elevations of the diabetic type. Raab and Strauber[6] compared the glucose tolerance curves of 12 normal persons, 12 diabetics, and 10 patients with parenchymal jaundice. They showed that both after glucose and after adrenalin, the blood sugar response in diabetes and parenchymal jaundice are similar. Soskin, Allweiss, and Mirsky[7] demonstrated that in a depancreatized dog receiving a constant injection of insulin plus dextrose, just sufficient to maintain the blood surgar at a constant level, the dextrose tolerance curve becomes definitely diabetic in type after administration of diphtheria toxin; their interpretation is in terms of liver function with toxemia.

One patient (Case 66) with a clinical and laboratory diagnosis of diabetes developed jaundice and gastro-intestinal complaints which warranted operative treatment. Exploration revealed no primary biliary tract disease, but an infectious cirrhosis of the liver. A cholecystogastrostomy was performed, and since then he has been asymptomatic. His diabetes has never been severe enough to require insulin either before or following operation, and in January, 1942, 13 years after his operation, he has gotten along well on dietary regimen alone. One would question that this man had true diabetes. The point to emphasize is restatement of the fact that a diagnosis of true diabetes in association with what is apparently gallbladder disease should not be accepted unless glycosuria and persistent hyperglycemia are present.

If it is true that jaundice is likely to affect the severity of diabetes or to cause diabetes, then it should be true that patients in this series of gallbladder cases, who have had jaundice on one or more occasions, should show in the later course some evidence of this effect. There are 15 patients in this series who were jaundiced one or more times before operation, and who are subjects for comparison of their insulin requirements one year before and one year after operation. Like those who did

not show jaundice, these 15 patients required on the average, no more or no less insulin before operation than after operation, namely, 14 units. This total average insulin dose is considerably smaller than that required for those who were not jaundiced (14 units *versus* 21 units) and represents, on the whole, a group with less severe diabetes than those without jaundice.

Cholecysto-enterostomy, with carcinoma of the head of the pancreas, and removal or drainage of the gallbladder, with a neoplasm of that structure, afforded palliation not only of jaundice but frequently also of pain for as long as three to ten months in carcinoma of the pancreas head, and even longer in carcinoma of the gallbladder. The diabetic's course in this respect is essentially no different from that of the nondiabetic. Five patients with carcinoma of the pancreas who were operated upon for release of common duct obstruction and who were dead in January, 1942, lived an average period of 11 months after the first appearance of symptoms referable to that disease.

CONCLUSIONS

1. The result of surgical treatment of gallbladder disease in the patient with diabetes is equally as good as in the patient without diabetes.

2. Complete relief of symptoms was afforded in 77 per cent of 65 cases with benign gallbladder disease; partial relief in 12 per cent; and no relief in 11 per cent.

3. Operative mortality for the entire series, including benign and malignant lesions, is 3.9 per cent. For those with benign gallbladder disease, including acute and chronic lesions and complications, the operative mortality is 4.6 per cent.

4. The eradication of a diseased gallbladder will neither heal nor lessen the severity of diabetes, as measured by the insulin requirement one year before, as compared with one year after operation.

5. The presence or absence of jaundice in the diabetic patient with benign gallbladder disease does not affect the severity of the diabetes subsequent to successful operation.

6. The incidence of complications in benign gallbladder disease is considerably greater in the diabetic than in the nondiabetic. Twenty-two per cent of the benign gallbladder lesions came to operation with complications which included hydrops, empyema, gangrene, perforation and pancreatitis. Except for the immediate operative mortality in the group (14 per cent), the result of surgical treatment was excellent.

7. Perforation of the biliary system by calculi occurred in 14 per cent of all patients with benign gallbladder disease coming to operation. Two-thirds of the perforations were in acutely inflamed or emypemic gallbladders.

8. The patient with gallstones should be "operated upon when the conditions of time, place, surgeon and physician are propitious." The indication for operation must be based upon the dangers incident to gallstones in the

nondiabetic, the greater susceptibility to perforation and the greater liability to arteriosclerosis in the diabetic.

9. The indication and results of surgical treatment of the diabetic patient with an obstructive malignant lesion of the gallbladder or pancreas, is essentially the same as in the patient without diabetes. Marked diminution in insulin requirement will sometimes be seen in patients with these lesions, and in obstructive jaundice following operative release of the obstruction.

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ABSORBABLE COTTON, PAPER AND GAUZE*

(OXIDIZED CELLULOSE)

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FOR AT LEAST THIRTY YEARS, in the Department of Surgery of Columbia University, there has been a continuing interest in the possibility of finding a relatively nonirritating, absorbable material. Many chemical products were tested, but few offered enough promise to justify further investigation. Recently (1935) Dr. Hans Clarke, of the Department of Biochemistry, suggested polyvinyl acetate, which proved nonabsorbable in its fully esterified condition and too irritating after partial or complete hydrolysis. In 1941, he proposed a trial of oxidized cellulose which had just been prepared by Kenyon, and his collaborators[2, 3] (U. S. Pat. No. 2,232,990), Eastman Kodak Research Laboratories.†

The experiments here described, though less extensive than could be desired, are now reported, in view of the interesting and important results secured with the same material by Dr. Tracy J. Putnam,[4] of the Department of Neurology.

To the surgeon it is of some interest whether such a product is in the form of cotton, gauze or paper. The material first investigated was in the form of cotton; later, some oxidized paper, prepared by the same method, was secured, also through the kindness of Dr. Kenyon. This was in response to our desire for a nonirritating absorbable membrane which might be used to fill defects in such mesodermal structures as tendon sheaths and blood vessels. The cotton naturally suggested the possibility of hemostasis with a packing which would not have to be removed. This idea has been further extended to embrace oxidized gauze.

The introduction of these materials into the tissues of animals was, therefore, undertaken. The product used had been prepared by oxidizing long-fibered cotton with nitrogen dioxide for seven hours. It had the appearance of ordinary surgical cotton, slightly off white, and somewhat more friable. It was, as reported by Yackel and Kenyon,[2] soluble in dilute aqueous alkalis because of extensive carboxyl group formation during oxidation. It was, therefore, thought that the product should also be capable of gradual dissolution in the tissue fluids in contact with relatively undamaged tissue. It did not withstand sterilizaton in the autoclave, but it kept its tensile strength when boiled in water for three minutes. The sterilization so obtained

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† The writer wishes to express her appreciation of the information regarding this substance communicated by Dr. Kenyon, in advance of publication (1942).

is obviously not enough for use in human surgery, since spores would not be destroyed by this method, but if the material should prove useful this difficulty might be overcome, possibly by preparation and packing under sterile conditions.

Ten samples of oxidized paper were available a year later. These had been oxidized: (A) 1 hour; (B) 2 hours; (C) 3 hours; (D) 4 hours; (E) and (F) 5 hours; (G) 21 hours; (H) 29 hours; (I) 45 hours; and (K) 69 hours. The longer the oxidation the greater was the shrinkage of the paper from its original size, the greater the brittleness and surface glazing and the less the tensile strength, although the fiber structure was grossly maintained. Microscopically, however, possibly through further degradation in the process of paraffin embedding and staining, the fibers of the cotton and gauze do not have the usual glassy appearance with central canal seen in unoxidized material, but appear as homogeneous eosinophilic bands, difficult to distinguish from coagulated protein.

Preliminary experiments suggested that the more highly oxidized samples, which were more acid, were more irritating to the tissues, and as, after boiling, these samples tore very readily when wet, sample H, I and K were soon discarded. Sample G, 21-hour oxidation was used in the first series, since it was thought that the less oxidized samples might not be absorbed. Later, however, through a chance selection, it was found that sample D was absorbed, and this, after only four-hours oxidation, had considerably more tensile strength than sample G. The papers, kept for a year at room temperature in the laboratory, continued to change slowly, and samples G through K at the end of that time were so brittle and parchment-like that they could no longer be used.

In the first group of experiments the cotton, seven-hour oxidation, was introduced into the abdominal muscles of cats and dogs. This, as was the case in all of the procedures, was done with the animal under nembutal anesthesia, and with strict asepsis maintained. The abdomen was opened through a right rectus incision, and the parietal peritoneum over the transversalis exposed by gentle retraction. It was then incised, and a pocket made in the muscle by blunt dissection. The sample, a fragment about 4 x 3 x 2 mm., was introduced. The pocket was closed by a black silk suture in the peritoneum and fascia, placed at some distance away from the implanted cotton. The implantation was also as far as possible from the incision in the abdominal wall, to avoid risk of skin contamination. Some of the animals employed were those used in the introductory course in Second Year Surgery, and had, in addition to the deliberate introduction of the experimental foreign bodies, other procedures in the abdominal cavity. These, however, were clean operations. Nevertheless, the danger of contamination in this group was considered greater than in those done without the presence of numerous observers and with unskilled assistance. The results are shown in Table I. It will be seen that in eight cases, at and after four weeks, the cotton was absorbed, with varying degrees

TABLE I

OXIDIZED COTTON IN MUSCLE—SEVEN-HOUR OXIDATION

S.P.No.	Days	Absorption		Reaction	Comment
		Gross	Microscopic		
20121	4	0	0	0	Animal dying.
20129	9	0	0	Polys. Mild	
20050	14	±	±	F.B. Mild	
19093	28	+	+	Scar tissue	Class.*
19094	28	+	±	F.B. Very mild	Class. Tiny fragments microscopically.
19095	28	+	+	Polys. Abscess	Class. Abscess around suture.
19096	28	+	+	Polys. Intense	Class. Abscess around suture.
19110	28	+	+	Polys. Intense	Class.
19112	28	+	+	F.B. Mild	Class. Polys. around suture.
20613	35	+	+	Scar tissue	Suture in scar.
20614	35	+	+	F.B. Moderate	

of foreign body reaction and phagocytosis. Solution, in the true sense, is likely to be retarded in the presence of damaged tissue, where the buffering power of the fluids is reduced. The lack of reaction in the four-day test (Fig. 1) was thought probably due to the fact that the animal was failing steadily and perhaps was unable to produce any tissue response to the irritant.

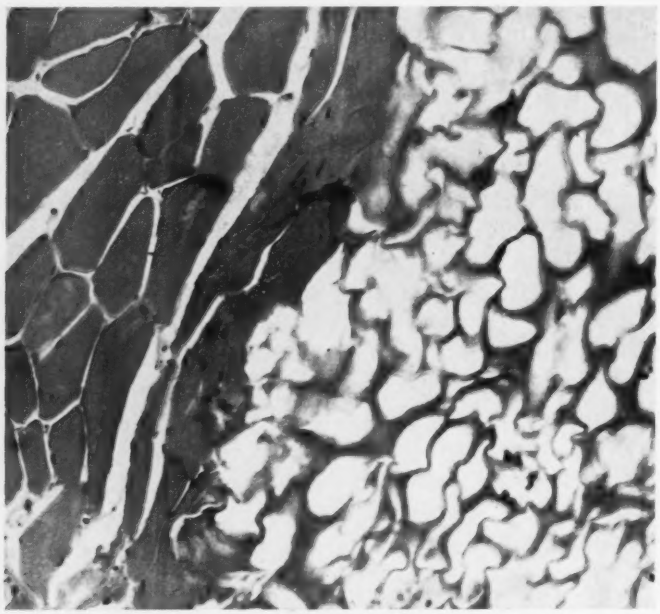

FIG. 1.—S. P. No. 20121: Photomicrograph. Oxidized cotton in muscle, four days. No reaction. This shows the appearance of the material when it has not been altered by the tissues, but after paraffin embedding, sectioning and staining.

In one case, S. P. No. 19094, a few microscopic fragments were found surrounded by giant cells. In the 14-day case there was partial absorption grossly and microscopically. There was in every case difficulty of distinguishing between a tissue reaction which might have been due to the cotton and that obviously expected from the presence of the black silk suture. The

* Where "Class" appears in Tables I and II, it refers to an animal used in class instruction.

suture was, of course, necessary for two reasons: First, to insure the sealing of the material in the pocket in the muscle; and, second, to mark the site.

The paper which was introduced into the muscle was sample G, oxidized 21 hours. Four of these animals were those in which the cotton had been introduced on the opposite side. It will be seen from Table II that in all but two of the seven implantations the paper was absorbed. The first case was that of the animal who lived only four days. The other was one of three animals, used also for class study, and sacrificed at the end of 26 days. The bulk of the material had been absorbed in this case, and what remained was microscopically fragmented. The nine-day absorption was a surprise, and it is possible that the wrong plane of section may have been taken, since the paper was very thin. None was seen grossly, however, on transillumination.

TABLE II
OXIDIZED PAPER IN MUSCLE—21-HOUR OXIDATION

S.P. No.	Days	Absorption		Reaction	Comment
		Gross	Miscoscopic		
20121	4	0	0	0	Animal dying.
20129	9	+	+	F.B. Mild	
20150	14	+	+	F.B. Very mild	
20342	26	+	+	F.B. Mild	Class. Polys. around suture.
20343	26	±	0	F.B. Mild	Class. F.B. reaction around suture.
20344	26	+	+	F.B. Mild	Class.
20613	35	+	+	F.B. Very mild	

Further detailed work is obviously desirable to determine as nearly as possible the usual absorption time, but it is clear that the material is absorbed and that it excites a foreign body reaction which is not necessarily excessive. Again, it should be emphasized that the more the tissue damage, by operative trauma or bacterial action, the greater the inflammatory reaction and possibly the retardation of true solution of the material in the less alkaline medium.

The next tissue investigated was brain, with the idea of the possible value of the cotton in hemostasis. We are indebted to Dr. James G. Galbraith for the meticulous care with which he introduced this material into the parietal lobes of cats. Through a midline incision in the shaved scalp the right temporal muscle was retracted and a trephine opening was made in the right parietal bone. This was enlarged by rongeur to 1.5 cm. in diameter. A linear incision was then made in the dura over the posterior part of the cerebral hemisphere and, with a bayonet forceps by blunt dissection, the cortex was split. A No. 19-gauge cannula was introduced into the brain, anteriorly and medially, to a 15-mm. depth, and a small bit of oxidized cotton, 4 x 3 x 2 mm., was expressed into the subcortical white matter. The dura was closed by interrupted, fine silk sutures, and the wound in layers with interrupted silk. One case was controlled by also introducing, somewhat posteriorly, a piece of temporal muscle of about the same size as the cotton.

The results of these experiments may be seen in Table III. In S. P. Nos. 21218 and 21219 the cotton had been soaked in soluble thrombin[4] provided

TABLE III

OXIDIZED COTTON IN BRAIN—RIGHT PARIETAL LOBE—SEVEN-HOUR OXIDATION

S.P. No.	Days	Absorption		Reaction	Comment
		Gross	Microscopic		
20576	10	±	0	F.B. Mild	
21326	18	+	±	F.B. Intense	
21327	18	±	±	F.B. Intense	
21320	21	±	0	Polys. Necrosis	
21321	21	+	±	F.B. Mild	
20698	42	+	+	F.B. Mild	
21218	43	+	+	Inflam. Trace	Soaked in thrombin. Muscle control.*
21219	43	+	+	F.B. Trace	Soaked in thrombin.

by Dr. Tracy J. Putnam of the Department of Neurology. In these two cases there was less reaction to the damage than in any of the others. Both were 43 days after operation. It will be seen that in all instances there was some tissue reaction (Fig. 2), but this was mild in five out of eight, and was also elicited by the muscle implant. Absorption was incomplete at ten days. All three six-week cases showed complete absorption. In the 18- to 21-day period there was some variation. Unfortunately no four-week cases were done in this group, but it can be said that the material is absorbed in the brain some time between three and six weeks, is not unduly irritating, and provokes a minimum of glial reaction. All these animals recovered well from the procedure after a few days of lethargy, and showed no focal nor general signs immediately before autopsy.

In five instances oxidized paper was tested in relation to the dura. Four

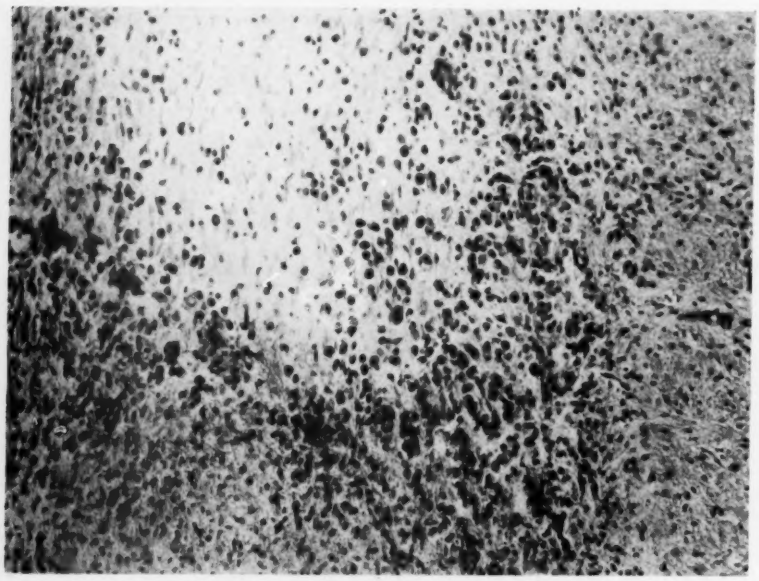

FIG. 2.—S. P. No. 20698: Photomicrograph. Oxidized cotton in brain, 42 days. None of the material remains. No polymorphonuclear leukocytes present. A few hemosiderin-laden phagocytes and slight glial proliferation.

* Muscle Implant Control: Muscle had been absorbed. Reaction the same as to the paper, *i.e.*, hemosiderin in phagocytes, slight glial proliferation, no multinucleated giant cells.

TABLE IV

S.P. No.	Days	Size in Mm.	Hours Oxidation	Absorption: Gross	Absorption: Microscopic	Reaction	Comment
OXIDIZED PAPER—SUBDURAL							
20697	42	10 x 10	21	+	+	F.B. Mild	
21218	43	5 x 5	4	+	+	F.B. Mild	3 mm. gap in closure, dura.
21219	43	5 x 5	4	+	+	F.B. Mild	
OXIDIZED PAPER—EPIDURAL							
21327	18	2 x 5	4	+	+	Abscess	Bone wax.
21321	21	2 x 5	4	+	±	F.B. Mild	

of these animals were those in which the cotton pledget had also been put in the brain. In three cases the paper was placed on the surface of the brain, twice over the puncture wound at the site of the cotton introduction, and once on the uninjured surface. The dura was then closed over the material with fine interrupted sutures. In two cases the paper was placed on the surface of the dura, over the opening which had not been sutured, thus making the closure in the wound. In both of these cases the animal also had the brain wound.

As will be seen in Table IV no paper was found in the three cases where

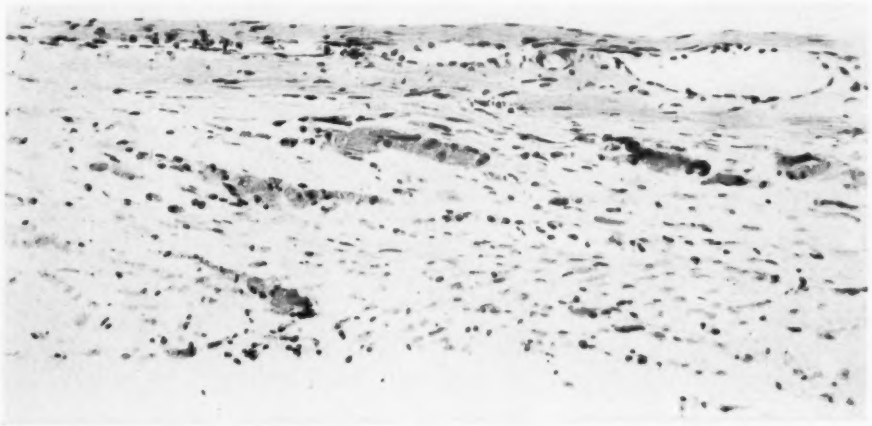

FIG. 3.—S. P. No. 21218: Photomicrograph. Oxidized paper, subdural, 43 days. No material remains. Few phagocytes present.

it had been placed between the brain and the dura. The incision in the dura was cleanly healed, there was no adhesion between the brain and the dura, and both surfaces were smooth and glistening. The disappearance was grossly complete. Microscopically, there were no polymorphonuclear leukocytes present and no multinucleated giant cells, but there were phagocytic mononuclear cells in the dura, often laden with hemosiderin (Fig. 3).

In the two cases where the dura had not been closed, and the paper placed over the defect, there was clean wound healing in one, but in the other there was an epidural collection of thick reddish-brown exudate in which gross particles of bone wax were seen. Microscopically, no paper was recognized in either of these instances, but there was a foreign body

TABLE V
OXIDIZED PAPER IN KNEE JOINT—FOUR-HOUR OXIDATION

S.P. No.	Days	Size in Mm.	Absorption: Gross	Absorption: Miscoscopic	Reaction	Comment
21326	18	5 x 3	+	+	F.B. Mild	Trichinae
21327	18	5 x 3	+	0	F.B. Mild	
21320	21	5 x 3	+	+	F.B. Very mild	
21321	21	5 x 3	+	+	F.B. Very mild	

reaction which might have been due to the material, but also might have been associated with the bone wax. The repaired deep surface of the dura was smooth, however, and there were no adhesions between this and the brain. Since, microscopically, some foreign body reaction was found in all these wounds of the dura, it is not possible to say that the paper disappeared by true solution. However, in no instance was it so irritating that adhesions formed between the dura and the brain.

Because of our original hope of finding something to use as a non-irritating membrane for repair of tendon sheaths, and because of the dif-

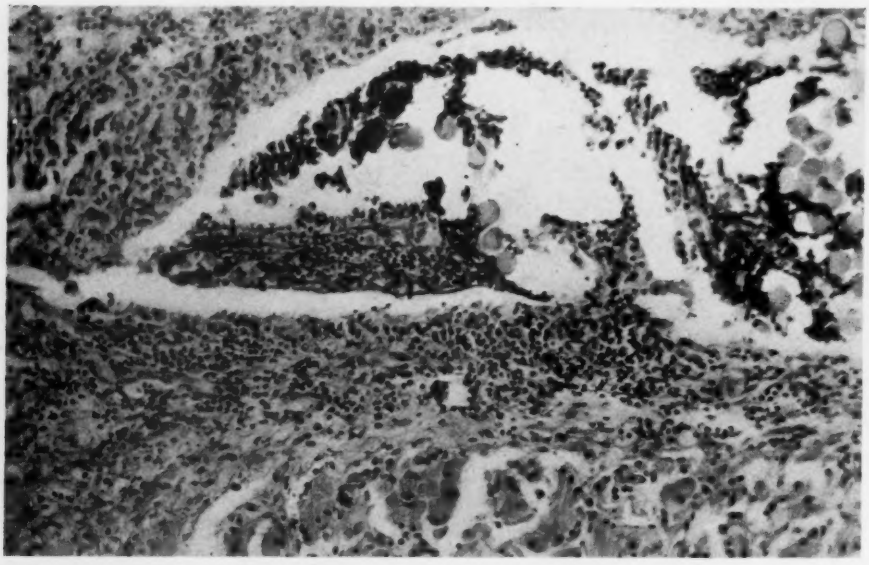

FIG. 4.—S. P. No. 21327: Photomicrograph. Oxidized paper in knee joint, 18 days. A fairly intense inflammatory reaction to the suture is seen in the upper portion of the photomicrograph, and a mild foreign body reaction to the paper in the lower portion.

ficulty of testing this out in animal tendon sheaths, the knee joint was used to determine the effect of the material on synovial tissues. The animals used were those who had also had, at the same operation, the craniotomy. This made them unusually suitable for joint surgery, since, for the first few days after operation, their lethargy caused them to avoid undue use of the extremity. The knee joint was opened through a lateral incision, and a strip of paper, sample D, four-hour oxidation, 4 x 2 mm., was introduced into the suprapatellar bursa. An effort was made in closing the defect with three interrupted eye silk sutures, not to place these in the synovial

membrane, but just outside. The skin was closed with four interrupted black silk sutures. As will be seen in Table V, at autopsy, in the first 18-day case no trace of the foreign body was found free in the joint where it had been placed, nor in the tissues outside. The joint lining was smooth, glistening and not injected, and the sutures lay well outside the cavity. There was, microscopically, a mild foreign body reaction but no evident paper fragments. An incidental finding was the presence of minute encysted trichinae larvae. In the second 18-day case there was, just to the lateral

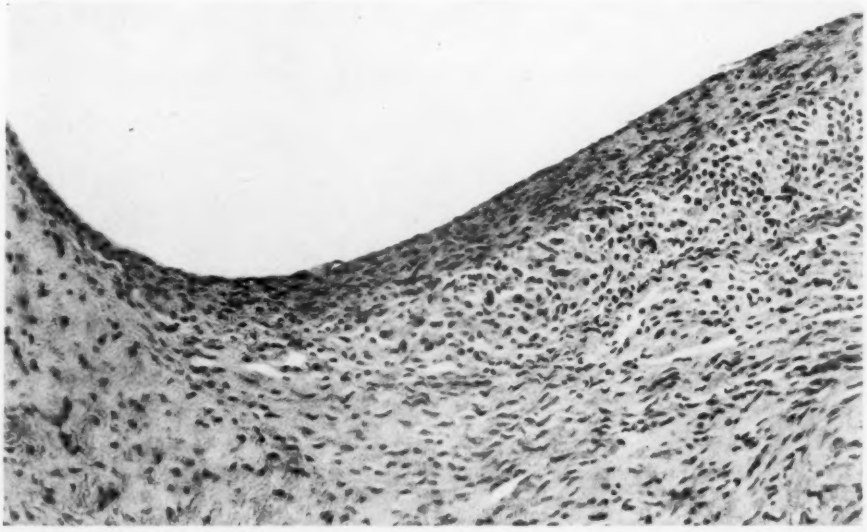

FIG. 5.—S. P. No. 21321: Photomicrograph. Oxidized paper in knee joint 21 days. There is slight thickening of the synovia, with a few lymphocytes and phagocytic cells.

side of the upper portion of the patella, an oval, slightly elevated pink zone, 6 x 3 mm. Otherwise the joint lining was smooth and glistening, without injection. There was no exudate. Microscopic examination of the red zone showed a localized mass of the material with a mild foreign body reaction, less intense than that around silk sutures in the same preparation (Fig. 4). In the two 21-day cases the knee joint showed no gross signs of inflammation and only a trace of foreign body reaction microscopically (Fig. 5). No material was found. In these four instances, at least, therefore, we have no evidence that the material causes undue inflammatory response in the joint such as might be followed by adhesions.

Oxidized cellulose in the form of gauze was then investigated. The shrinkage of this material is shown in Figure 6, and it is interesting that the texture of the oxidized samples is smoother and more silky than the original gauze, and, naturally, with the shrinkage, finer meshed. The 16-hour sample, however, was quite friable, and was only used once. The procedure was to deliver the omentum through a right rectus incision, onto warm moist pads. A square of gauze, 1.2 cm., was then laid on the surface, the omentum

TABLE VI

OXIDIZED GAUZE ON PERITONEAL SURFACE

S.P. No.	Days	Hours Oxidized	Absorption		Reaction	Comment
			Gross	Microscopic		
21364B	6	7	±	0	Polys. Intense	Second trauma.
21364A	7	7	+	±	Polys. Intense	More reaction to suture.
21329	11	7	+	+	F.B. Moderate	
21347	14	16	+	+	F.B. Mild	
21402	20	7	+	+	F.B. Trace	

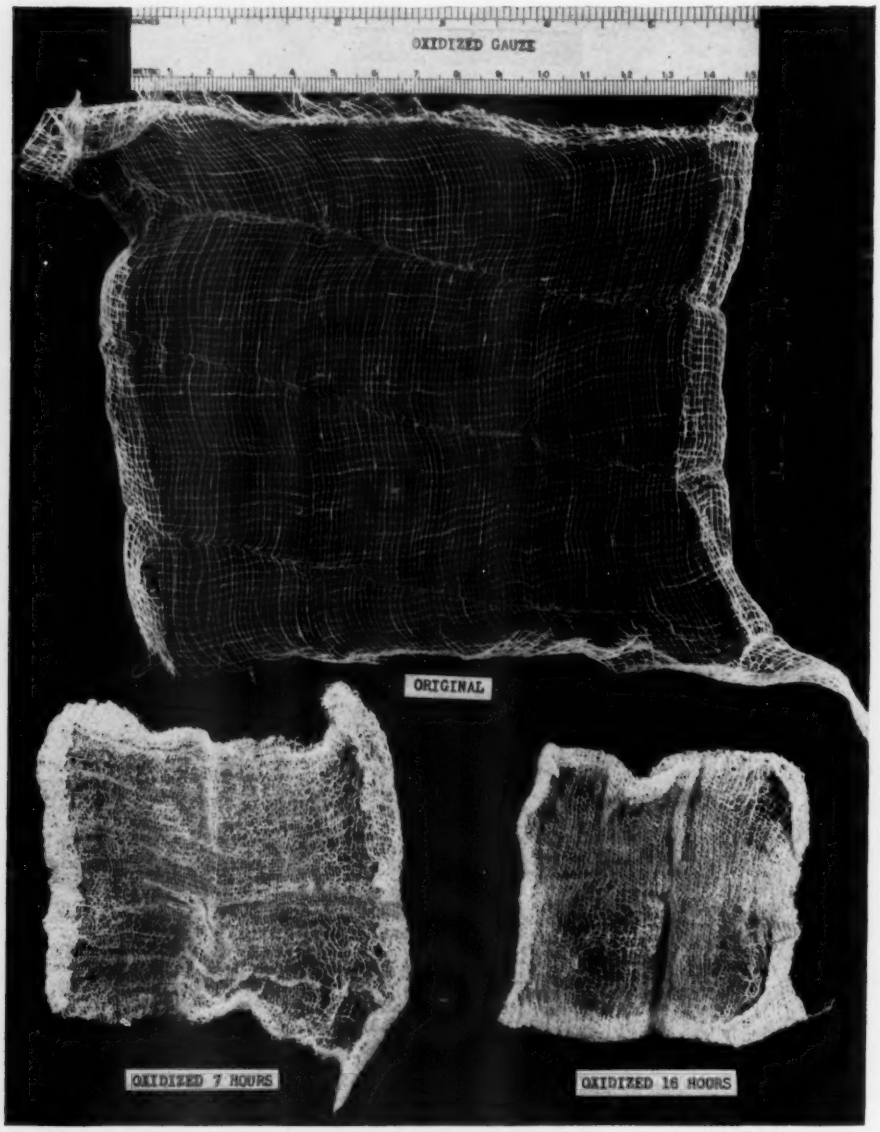

FIG. 6.—Photograph of three samples of gauze, all originally approximately the same size. Shrinkage following oxidation is illustrated.

folded over it, and tacked down with silk sutures which did not pass through the material. In the 11-day case the sutures used were a thread ravelled from the edge of the gauze itself. The results are shown in Table VI. The first case listed, six-days, is the same animal as the seven-day experiment. An exploratory operation was performed, seven days after the first procedure. The omentum was found to be thickened in the neighborhood of the marking sutures. This portion was amputated, after suitable hemostasis had been secured by ligature, and a second piece of gauze, rolled this time instead of flat, was placed in the folded, already traumatized. omentum. On reexploration at six days much greater thickening was found than previously, but there were no other signs of inflammation about the gauze. Around the ligatures, however, there was redness as well as swelling. The gauze appeared as a sticky, light brown fluid and semi-

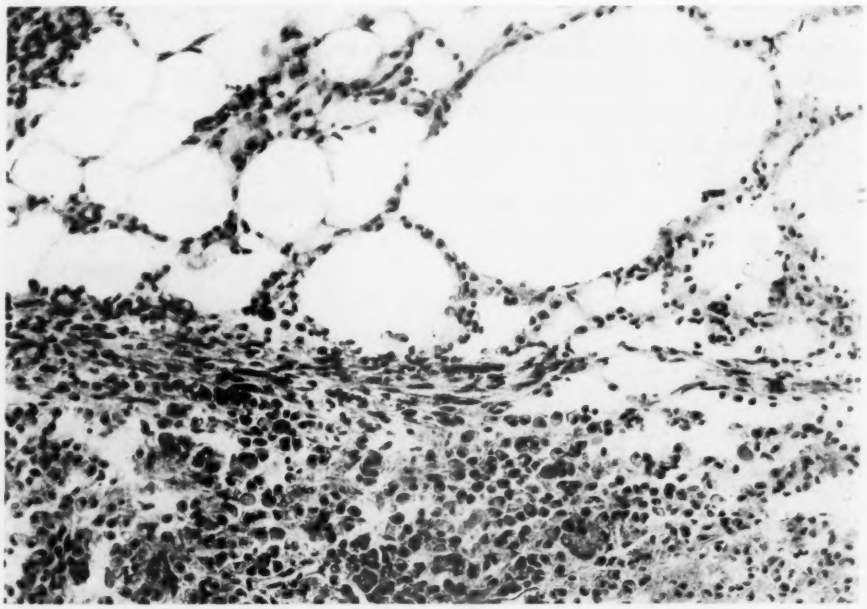

FIG. 7.—S. P. No. 21329: Photomicrograph. Oxidized gauze in omentum, 11 days. No material remains. Mononuclear and multinuclear phagocytic cells are seen and some foamy fat cells.

solid material lying in a smooth cavity. Microscopic examination showed an intense inflammatory reaction both to the foreign body and the ligatures, with polymorphonuclear leukocytes present in each case. More dilated blood vessels were seen about the sutures than about the gauze. At 11, 14 and 20 days no gauze remained. There was thickening in the omentum in each case, but no more inflammatory reaction than might have been expected from the operative trauma and the sutures (Fig. 7).

SUMMARY

Oxidized cellulose in the form of cotton, paper and gauze was found to disappear in muscle, brain, dura, joint and peritoneum of dogs and cats.

Control experiments of unoxidized material were not made because of the universal experience that gauze and cotton are not absorbed, and our familiarity with the reaction of the tissues to these materials.

In all but one instance there was some tissue reaction, and in this case the cotton was not absorbed. How much the disappearance of the material is due to true solution and how much to solution after digestion by phagocytes it is not possible to say. Not much proliferation of connective tissue, nor of glia was found. No adhesions were formed between the dura and the brain or within joints.

CONCLUSIONS

A relatively nonirritating foreign material, oxidized cellulose, has been tested. It is hoped that, after further observations to determine the oxidation time associated with the most favorable properties, this may be employed in hemostasis and possibly in protecting injured surfaces where a smooth membrane is desired in the final healing. For this latter use further work must be undertaken to determine the length of time the material maintains its physical properties in the tissues when it is interposed between two surfaces where adhesions are to be avoided.

The length of time of oxidation may well be related to the rapidity of absorption. A method of sterilization must be developed so that all danger of spore contamination is avoided, and the desirable physical properties of the material are not altered. It is suggested by earlier experimental work with celloidin in this laboratory by W. C. Clarke,[1] in 1916, that some of the reaction observed with samples of the new material may have been due to contact with the skin of the investigators. The material was handled to a considerable extent before it was boiled for use, and epithelial débris may have adhered to it. New samples, not fingered except with gloves, will be tried. The degree of irritation to the tissues from any cause, however, does not seem to be extreme, and is usually less than that from the nonabsorbable sutures so freely used in plastic work.

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THE USE OF THROMBIN ON SOLUBLE CELLULOSE IN NEUROSURGERY

CLINICAL APPLICATION

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PREPARATION OF THROMBIN.—The preparation of a relatively pure thrombin has been a recognized laboratory procedure since the work of Mellanby,[1] in 1933. His method has been greatly improved by Seegers,[2, 3] who, with his collaborators, has reported on its use in experimental surgery. The hemorrhage from a fresh incision across the surface of the liver or brain was controlled by a spray of the solution. Similar results have been reported by Lozner, *et al.*,[4] with the use of rabbit thrombin, prepared by iso-electric precipitation. These investigators found the application of moist pledgets to be more effective than a spray of the liquid preparation. As far as I am aware, the first attempts to use such a preparation for neurosurgical purposes were made by Karr and Ziff[5] at this institution. They prepared fresh thrombin from human plasma by a simple technic, and this proved of some value in cerebral surgery. According to the daily papers, a preparation of thrombin has been used by the Russian surgeon Kudryashev, but no references are available at present.

Preparations of thrombin which are highly active are now being manufactured according to the method of Seegers, and are, of course, far more convenient than the freshly prepared material. The thrombin comes in the form of a dry powder, easily soluble in water. A "clotting globulin" is also available, made from rabbit plasma. A globulin with thrombic activity, and a concentrated fibrinogen are being prepared on a large scale from human plasma.

The difficulty with fluid preparations has been that of application. The clot which is formed in less than a second with flowing blood is apt to be washed away before it can adhere, even though the flow is no more than an ooze. If the thrombin is applied upon pledgets of cotton, satisfactory hemostasis is secured under even adverse conditions, but hemorrhage usually begins at once if the pledget is removed.

By a fortunate coincidence, a new type of oxidized cellulose became available within recent months. The details of preparation of this material have been described by Yackel and Kenyon,[6] and Unruh and Kenyon,[7] and its properties are easily observed and of great interest. Physically, it resembles cotton wool. It will, however, slowly dissolve in slightly alkaline fluids. Frantz[8] has carried out experiments which show that it is absorbed from various tissues of experimental animals (including the brain) with practically no inflammatory reaction. This prepared cellulose disintegrates upon autoclaving. It may, however, be boiled for three minutes or kept in 70 per cent alcohol until needed.

An obvious next step was to use this material saturated with thrombin solution. Tiny pledgets, measuring approximately 20 x 5 x 2 mm. were prepared by teasing out and folding the wet cotton. They were kept in 70 per cent alcohol. When needed they were dried at the time of

A

B

FIG. 1.—A. Constant, profuse oozing from dural veins (arrows). Note pool of blood along edge of bone at bottom of picture.
B. Hemorrhage controlled and wound clean, two minutes after application of thrombin on soluble cellulose (arrows). The pool of blood has been removed, and now has reaccumulated.

operation, and dampened with thrombin solution, so that each contained approximately 500 units. (It is possible that less would suffice)

The most effective way of using these pledgets was found to be to tampon a bleeding point with moist cotton, and suck the latter dry. The pledget containing thrombin was then rapidly substituted for the tampon, and another piece of damp cotton placed on it. This, in turn,

was sucked dry. Even with active arterial bleeding; for example, during excavation of a meningioma, the second tampon could usually be removed within a minute, leaving the soluble cellulose solidly clotted.

This technic has been used in 30 operations of various types, with great satisfaction. In five instances, it appeared to be more effective than muscle. One of these was in a case of subfrontal meningioma, in which bleeding was a major problem. Another instance was in an operation of chordotomy in a patient with sarcomatosis, in which there was stubborn bleeding from peridural veins. The material saves much time in dealing with small oozing points on pacchionian granulations or from dural veins (Fig. 1). It renders trigeminal root section a far easier procedure.

In most of these operations, the thrombin preparation made by Parke, Davis & Company, essentially by the method of Seegers, *et al.*, was used. Lederle's "clotting globulin" and thrombin from human plasma, prepared by Cohn and Edsall,[9] has also been employed with similar results. An accurate comparison between the various substances is impossible to make at present.

Obviously, other uses for similar preparations suggest themselves. Thin sheets of such treated cellulose might be used to control bleeding from the cut surface of parenchymatous organs; for example, the bed of the gallbladder. A similar gauze might be used in skin grafting. For first aid use in the field, an antiseptic such as sulfapyridine, penicillin or or gramicidin might be added to such tampons for packing deep wounds. Sulfapyridine has been added to the pledgets described above without affecting their hemostatic properties.

Appreciation is herewith expressed to the Lederle Laboratories, who supplied the clotting globulin, to Parke, Davis & Company, who supplied the Seegers' thrombin, and to Doctors Edwin Cohn, John Edsall and S. Howard Armstrong, who supplied the thrombin from human plasma. I am equally grateful to the Eastman Kodak Company which supplied the soluble cellulose. It was prepared by Mr. C. C. Unruh and Dr. W. O. Kenyon, and brought to my attention by Dr. Hans Clarke.

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CONVULSIONS DURING GENERAL ANESTHESIA*

REPORT OF TWELVE CASES

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IT IS NOT OFTEN that there is justification for emphasizing a single symptom when considering the nature of a pathologic process but in the case of convulsions that occur during anesthesia there may be some excuse. A convulsion from whatever cause is always a dramatic event and when it occurs during an operation it is frequently the first and, indeed, may be the only recognized sign of what is believed to represent a serious and potentially fatal state.

The problem of convulsions during anesthesia has been largely the concern of the anesthetists; thus, the importance of discussing it before a surgical society may require some explanation: First, let it be said, that under any circumstances the surgeon cannot neglect his share of the responsibility for the safety of his patient, even though the anesthetist be an expert. Furthermore, it has become evident in the case of convulsions that there are probably many factors in the care of the patient before, during and even after operation that are as important as the anesthetic and which are largely the surgeon's responsibility.

The phenomenon in question is quite distinct from the familiar clonus or tremor seen during the induction of anesthesia, principally with ether, and it is not to be confused with the transitory muscular twitching that rather frequently is seen in later stages of the anesthesia, when oxygen intake is limited. The attack generally develops with twitching about the eyes and mouth when the patient is deeply under the anesthetic. There follow spasmodic contractions of the limbs and most of the muscles of the body, resulting in generalized and usually violet convulsive epileptiform movements.

As a basis for discussion of the subject a study has been made of 12 patients in whom convulsions occurred out of a total of about 75,000 subjected to general anesthesia during the past ten years at the New York Hospital. Excluded from the study are those instances in which convulsions developed after anesthesia and those occurring during "local" or nitrous oxide anesthesia. The latter group is omitted largely because the etiology of convulsions, postoperative encephalopathy and death with nitrous oxide anesthesia seems to be no longer a mystery but is almost universally accepted as due largely to anoxia of the brain.[1] On the other hand this group is no doubt closely related to the cases to be discussed since anoxia in all prob-

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ability also plays the major rôle in convulsions during other forms of general anesthesia.

It is not so much, then, the convulsions themselves but the underlying state of which they are the manifestation that is of chief concern. That this is true is evidenced by the high mortality that accompanies the condition; it is too high to be accounted for by the occurrence of convulsions alone. It is variously estimated that the mortality is between 18 per cent[2] and 50 per cent.[3] The convulsions developing infrequently, as they do, and often without warning, have usually found the surgeon unacquainted with their importance and unprepared to deal with the problem intelligently.

The subject was introduced in England, in 1927, by the simultaneous reports of Wilson[4] and Pinson.[5] Other reports of isolated cases followed in rapid order and, because all of the convulsions occurred during ether anesthesia, they came to be known as "ether convulsions." The inference was that the phenomenon was somehow related to the specific property of ether and, since but a few cases had been reported or could be recalled prior to that time,[6–9] it was thought that some impurity existed in the ether which had not been present previously. The probability is that the condition existed before but went unrecognized, and we now know that convulsions and other cerebral complications occur not alone with ether but with other general anesthetics as well.[1, 2, 10–18] In 1937, Lundy[2] reviewed the subject tabulated 144 cases largely from the literature, and listed a number of possible etiologic factors. A review in 1941, by Monroe and Benjamin,[18] disclosed 168 cases reported.

Few seem to have had experience with more than one or several such cases, and too few details are presented in many of the reports. This has increased the difficulty of studying the nature of the convulsions and resulted in a multiplicity of ideas regarding their etiology. The conditions under which the convulsions occur are difficult to evaluate at best, and particularly difficult to duplicate in every detail for experimental study. Furthermore, there is a dirth of information from autopsy studies of such cases. A survey of the reported cases emphasizes the great variability in the circumstances under which the convulsions occur; in fact, the only apparent common denominator in all cases is an operation in which a general anesthetic is employed. Recent essayists on the subject have focused their attention largely on the single factor of anoxia in the production of which both the condition of the patient and the nature of the anesthetic agents play equally important rôles.[19–26]

The following 12 case reports are of patients who developed convulsions during general anesthesia within the past ten years at the New York Hospital. Interest in the problem was aroused when one of us (Ray) observed the convulsions and postoperative sequelae to be reported in the first case. Through the assistance of the Department of Anesthesia it was arranged for one or both of us to be called to observe the convulsions that occurred in the other patients, or to appraise the circumstances soon

after the convulsions had occurred. Thus, it was possible to obtain fairly uniform and complete information about all the patients, from which certain deductions may now be made.

CASE REPORTS

Case 1.—H. F., female, age 36, was admitted, in April, 1933, with a subsiding acute cholecystitis. The past history was unremarkable. The patient was obese. Blood pressure 200/120, but EKG showed only left axis deviation. Blood urea nitrogen and routine laboratory tests were normal. After the acute episode had subsided, cholecystectomy and appendicectomy were performed. Preliminary medication of morphine 0.010 grams and atropine 0.0004 grams was given. Anesthesia was induced with ethylene and oxygen and maintained by the addition of 50 cc. of ether vapor, using a closed mask. A "gallbladder bench" was elevated to improve the operative exposure. The patient's condition was satisfactory for 90 minutes, until the wound was being closed when, without any warning changes, twitchings began in the face. Rhythmic clonic movements appeared over the entire body, being more marked on the left side. Anesthesia was discontinued and closure completed. Oxygen was administered. Six hundred cubic centimeters of blood was removed by phlebotomy, which reduced the blood pressure from 185/98 to 115/80. Convulsions lasted 35 minutes. In the first six hours postoperatively four five-minute seizures occurred. Complete consciousness was not regained for 12 hours, and the patient remained restless and mentally sluggish for another 12 hours. A left hemiparesis was present and the patient complained of paresthesias on the left side. There was a sharp elevation in temperature the first two days. Râles were present in both lungs, and there was increased respiratory rate and dusky color for three days. There was 4+ albumin in the urine on the fourth day. The hemiparesis partially resolved, but eight years' follow-up reveals a residual weakness of the left lower extremity. An electro-encephalogram made eight years postoperatively showed "a borderline record probably normal."

COMMENT.—It was believed at the time that the convulsions and subsequent hemiparesis were the result of a cerebral vascular accident but it is possible for focal signs to develop in the presence of generalized cerebral anoxia. Factors which may have contributed to the development of convulsions in this patient are cardiovascular disease and poor position on the operating table, resulting from elevation of the "gallbladder bench."

Case 2.—J. B., female, age 30, six weeks postpartum, was admitted, in June, 1936, with chronic cholecystitis and cholelithiasis. A past history of urticarial reactions to certain foods and dust was obtained. Physical examination and laboratory findings were normal. Phenobarbital 0.030 grams was given the night before operation. Preliminary medication of morphine 0.010 grams and atropine 0.0004 grams was given. Anesthesia was induced with nitrous oxide-oxygen. Maintenance was with ethylene, oxygen, and 65 cc. of ether vapor, by closed mask. A "gallbladder bench" was elevated to improve the operative exposure. Cholecystectomy and choledochostomy were performed without technical difficulty. The patient's vital signs and general condition remained constantly good for 75 minutes, except that respirations were "jerky" and "irregular" at times. During closure of the wound generalized vigorous convulsions began rather abruptly. The anesthesia was stopped and closure completed. Oxygen was administered. Ten cubic centimeters of 10% calcium gluconate and 1 cc. of parathormone were given, but no immediate effect of this was noted. Convulsions lasted 40 minutes. Four hours were required to regain consciousness but convalescence was

otherwise satisfactory. During a five-year follow-up period no further neurologic disturbances developed. An electro-encephalogram at the end of five years was normal.

COMMENT.—Factors which may have contributed to the development of convulsions in this patient are possible calcium and other nutritional deficiencies resulting from the recent pregnancy, plus the poor position on the operating table resulting from elevation of the "gallbladder bench."

Case 3.—C. K., male, age two, was admitted, in October, 1936, for repair of a cleft palate. During the first year he had been treated for rickets but at admission he was found in good general condition. Operation was postponed three days because of a rhinitis with low fever and a 24,000 leukocytosis. After preliminary atropine 0.00008 grams, anesthesia was induced and maintained with ether, by the open mask method. Later, ether was given by nasal catheter with a vaporizing machine. Anesthesia was deep. The pulse rate rose steadily from 120 to 180, and the respirations from 30 to 50 per minute. Eighty minutes after the induction of anesthesia, generalized convulsions began and lasted 30 minutes. Anesthesia was discontinued and oxygen administered. Fifty units of parathormone and an infusion of 6% glucose in normal saline were given. Temperature rose to 40°C. Consciousness was regained in three hours, but the patient was unmanageable for an additional six hours. Respirations were rapid for 36 hours and moist râles cleared gradually over the next three days. Carbon dioxide combining power and total serum protein taken during the convulsions were 45 volumes per cent and 6.8 per cent, respectively. On the first postoperative day serum calcium and phosphorus were 10.3 mg. per 100 cc. and 3.7 mg. per 100 cc., respectively. The recovery was otherwise uneventful, and the six-year follow-up has found no evidence of neurologic disorder.

COMMENT.—Factors to be considered as possibly contributing to the development of convulsions in this patient are: Youth; nutritional deficiency; recent respiratory infection; and relatively long and deep anesthesia.

Case 4.—M. S., female, age six, was admitted with perforated appendicitis and purulent peritonitis in August, 1938. The past history was unremarkable. The temperature was 39.6° C. (rectal), pulse rate 140, and leukocytosis 28,500. Four hundred cubic centimeters of 5% glucose in normal saline infusion was given because of dehydration. Preoperative medication was codeine 0.03 grams and atropine 0.0003 grams. Anesthesia was induced with ethyl chloride and maintained with 90 cc. of ether by open mask method. Fifty minutes after induction, during closure, a generalized convulsion began and lasted several minutes. Prior to this no noteworthy changes had occurred in the patient's general condition. Anesthesia was discontinued. Consciousness was regained in 90 minutes. There was a rise of one degree of temperature over that recorded preoperatively, and the respirations were 40 per minute for the first 36 hours. Thereafter recovery was uneventful. Analysis of the ether found "no impurities." A four-year follow-up has found no other evidence of nervous disorder, except an electro-encephalogram done three years later showed "a borderline record, probably pathologic."

COMMENT.—Factors to be considered as possibly contributing to the development of convulsions in this patient are: Youth; hyperpyrexia; toxemia; and dehydration.

Case 5.—T. W., male, age six, was admitted in September, 1938, acutely ill with appendicitis of at least 30 hours' duration. At the age of one he had had two generalized convulsions of unknown etiology which did not recur. One month before

admission, he sustained a mild concussion of the brain from which he seemed to have recovered. Temperature was 38° C. (rectal), and pulse 110. White blood cells were 21,000, but hemoglobin and red cell counts were normal. Preoperative medication was atropine 0.0002 grams. Anesthesia was induced and maintained with ether and oxygen through an open mask. Pulse rose from 100 to 160, and respirations were slightly irregular until 40 minutes after induction when facial twitching began. Generalized convulsions developed rapidly accompanied by irregular respirations and cyanosis. Oxygen was given and ether was reduced, but not discontinued, for 20 minutes to allow closure of the wound. The following medications were given—400 cc. of 5% glucose in normal saline intravenously; 1 cc. parathormone hypodermically; 10 cc. 10% calcium gluconate intravenously; and, finally, after two hours and 20 minutes of almost continuous convulsions, 0.6 grams of sodium phenobarbital intravenously, which was followed by a diminution in intensity and then cessation of the convulsions for two hours. Temperature rose to 42° C. (rectal) and pulse to 190. The urine contained 2+ albumin. Respirations remained rapid and the color slightly dusky. Consciousness was never regained and convulsions recurred intermittently. Frequently the seizures involved only the left arm. At first the deep reflexes were depressed but on the second day they were exaggerated and accompanied by bilateral extensor plantar responses. The spinal fluid contained 350 red blood cells and 0.075 Gm. per 100 cc. of total protein. The patient expired 40 hours postoperatively. No autopsy was performed. Analysis of the ether used showed impurities far below the U. S. P. standards and essentially the same as in a control from a freshly opened can.

COMMENT.—Factors to be considered as possibly contributing to the development of convulsions in this patient are: Youth; hyperpyrexia; toxemia; dehydration; and epileptic history.

Case 6.—A. H., female, age 40, was admitted, in August, 1940, with an exacerbation of chronic cholecystitis. The patient had had frequent convulsions until the age of six, but none thereafter. Her son, age six, had convulsive seizures. Parenteral fluids were given but with the increase in clinical signs operation was decided upon. Temperature was 39° C. hemoglobin 10 Gm., R.B.C. 3,400,000 and W.B.C. 11,600. Preoperative medication of morphine 0.010 Gm. and atropine 0.0004 Gm. was given. Anesthesia was induced with nitrous oxide and oxygen and maintained by the addition of ether vapor (closed mask). A "gallbladder bench" was elevated to improve the operative exposure. Fifty-five minutes after induction of the anesthesia, convulsions began about the face and soon spread over the body. The respiratory rate had gradually increased to 35 per minute prior to the convulsions. Anesthesia was deep and only a little ether was needed for maintenance during the next 40 minutes required to complete the operation. Convulsions of about one minute's duration recurred every two to three minutes for 30 minutes. During the seizures the respirations were jerky and the color dusky but in the free intervals the signs became normal. Oxygen and carbon dioxide, separately or in combination, had no appreciable effect but the condition improved shortly after the "gallbladder bench" was lowered. Recovery of consciousness was very slow, and for 36 hours the patient was irrational, incontinent, and had a temperature of 40° C. (rectal). Three blood transfusions were given to improve the low blood pressure. There were periods of dyspnea and moist râles in the lungs for three days; a roentgenogram showed evidence of pulmonary congestion. After the third day recovery was steady. An immediate postoperative uranalysis showed 3+ albumin and a few erythrocytes, but later examinations were normal. Blood calcium and phosphorus were normal. Analysis of the ether used showed essentially no impurities. During two years' follow-up there was no recurrence of the seizures but a memory

defect and a personality change, characterized by emotional instability and hysterical outbursts, were evident.

COMMENT.—Factors to be considered as possibly contributing to the development of convulsions in this case are: Epileptic history; mildly toxic state; secondary anemia; and poor position on the operating table, resulting from elevation of the "gallbladder bench."

Case 7.—L. R., female, age 27, was admitted, in March, 1941, for menorrhagia caused by tubal pregnancy. Over the preceding two years she had had about ten attacks of syncope without convulsions, which were ascribed to hysteria since they were associated with fatigue and emotional stress. The carotid sinuses were not hypersensitive to pressure. Diagnostic dilatation and curettage of the uterus was done under nitrous oxide, oxygen and ether vapor, by the closed mask method. Morphine and atropine had been given preoperatively. The anesthesia lasted 45 minutes and was uncomplicated. Two days later a tubal pregnancy was removed. Morphine 0.010 Gm. and atropine 0.004 Gm. were given before operation. The anesthesia was the same as before and given by the same anesthetist. Near the end of the 90 minutes' procedure, without warning, violent generalized convulsions began and lasted six minutes. The patient was returned to the horizontal from the Trendelenburg position and anesthesia promptly discontinued. Morphine 0.015 grams was given. Recovery of consciousness was delayed and there were signs of partial atelectasis of one lung which disappeared shortly with treatment. Recovery thereafter was uneventful. Electroencephalography on the fourteenth postoperative day showed waves of mixed frequency which probably represented a pathologic state.

COMMENT.—Factors to be considered as possibly contributing to the development of convulsions in this patient are: A history of syncopal attacks; recent operation; and poor position on the operating table resulting from lowering the head of the table (Trendelenburg position).

Case 8.—S. D., female, age 27, obese, was admitted, in August, 1941, with perforated appendicitis and purulent peritonitis. She had given birth to her third child 11 days before. Right lower quadrant pain had been present for eight days and generalized abdominal pain for 36 hours. Temperature was 39° C., pulse 120, respirations 26, hemoglobin 14.5 grams, hematocrite 46, and leukocyte count 26,000. Urine showed a trace of albumin and 2+ acetone. One thousand cubic centimeters of 5% glucose in normal saline was given intravenously before operation. Preoperative medication was morphine 0.010 Gm. and atropine 0.0004 Gm. Anesthesia was easily induced with nitrous oxide and maintained by the addition of 75 cc. of ether-vapor and oxygen, by closed mask. The patient was said to have considerable "ether tolerance." Blood pressure rose steadily from 130/80 to 160/98; the pulse from 120 to 135; but respirations remained about 30. Fifty minutes after induction, and 35 minutes after the incision, convulsions began in the chin and neck and soon spread generally. Cyanosis then appeared. The anesthesia was discontinued and 100% oxygen administered. One cubic centimeter of paraldehyde and 250 cc. of citrated blood were given intravenously. The temperature rose to 42.4° C. (rectal). Colonic irrigations of cool water were given. The convulsions lasted for 90 minutes; thereafter the patient's general condition became steadily worse and she died five hours after operation. No autopsy was performed. The following laboratory examinations were made during this time: Spinal fluid normal; blood culture sterile; blood sugar 123 mg.%; blood urea nitrogen 11 mg.% carbon dioxide combining power 52 volumes%; serum chloride 600 mg. per 100 cc.; total serum protein 6.7%; Cholesterol 234 mg.%.

COMMENT.—Factors to be considered as possibly contributing to the development of convulsions in the patient are: Recent pregnancy; hyperpyrexia; toxemia; and obesity.

Case 9.—J. G., female, age 36, was admitted to the hospital, in September, 1941, because of abdominal pain from an ovarian tumor (theca cell tumor). The physical examination was unremarkable but for obesity. The preoperative medication was morphine 0.010 Gm. and atropine 0.0004 Gm. Anesthesia was induced and maintained with cyclopropane plus 25 cc. of ether vapor. A uterine dilatation and curettage was followed by celiotomy and oophorectomy. Eighty minutes after induction of the anesthesia the respiratory and pulse rates increased. Ten minutes later hyperthermia was evident by a hot dry skin and the axillary temperature was 41.2° C. The anesthesia was discontinued, oxygen given, the operating table lowered to the horizontal from a rather high Trendelenburg position, and an intravenous infusion of saline started. The blood pressure fell steadily. Forty-five minutes after cessation of the anesthesia violent and generalized convulsions occurred and continued until death 12 minutes later. Autopsy disclosed congestion of pial vessels of the brain, pulmonary congestion, atelectasis of one entire lung, congestion of the kidneys, and petechial hemorrhages in the myocardium, pericardium and pleura.

COMMENT.—This is the only patient in whom there was an acute rise in temperature preceding the convulsions. Probably an unrecognized atelectasis was the most important factor in the development of the hyperthermia and the convulsions. Other factors to be considered as possibly contributing to the complications are: Obesity; and Trendelenberg position on the operating table.

Case 10.—H. F., male, age 44, was admitted to the hospital, in June, 1942, with what was thought to be gallbladder disease. A mass was present in the right upper quadrant of the abdomen. The hemoglobin was ten grams and the red cell count, 3.5 million. Uranalysis was normal. Serum prothrombin was 100%, and fasting blood sugar 99 mg.%. The red cell count rose to 3.9 million after a 500 cc. transfusion of citrated blood. Preoperative medication of morphine 0.010 Gm. and atropine 0.0004 Gm. was given. Anesthesia was induced with nitrous oxide and maintained by the addition of ether vapor, by the closed mask method. A large vascular neoplasm was found in the liver and only exploration was done. The blood pressure rose slowly from 110/65 to 130/75, and the pulse rate from 100 to 125. Anesthesia was deep. During closure of the wound 80 minutes after induction, facial twitchings began and were followed by generalized convulsions which lasted ten minutes. Anesthesia was discontinued and oxygen administered. Recovery from anesthesia was slow and the patient was partly irrational for two days. For five days a sharp febrile reaction was present and there was evidence of a right sided pneumonia with pleural effusion. Postoperative urine examinations all showed the presence of albumin. An electroencephalogram two weeks after operation showed "a borderline record, probably pathologic."

In December, 1942, a multiple posterior rhizotomy was done for relief of intractable pain. The same type anesthesia was used as before, but without complications. A subsequent autopsy disclosed a metastasizing hypernephroma.

COMMENT.—Factors to be considered as possibly contributing to the development of convulsions in this patient are: Secondary anemia; and too deep anesthesia.

Case 11.—R. S., female, age 40, was admitted to the hospital, in October, 1941, with chronic cholecystitis and cholelithiasis. Physical examination and routine laboratory tests were essentially normal except for the blood pressure of 170/110, and roentgenologic evidence of gallbladder disease. Morphine 0.010 Gm. and atropine 0.0004 Gm. were given preoperatively. Anesthesia was induced with nitrous oxide and maintained with ether vapor, by the closed mask method. Cholecystectomy and choledochostomy were performed. A "gallbladder bench" was elevated to improve the operative exposure. After 70 minutes of uneventful anesthesia twitchings began in the face, followed by generalized convulsions which lasted 15 minutes. Anesthesia was discontinued, oxygen administered and the "gallbladder bench" lowered. Sodium phenobarbital 0.13 grams was given intramuscularly, and 50 cc. of 50% glucose intravenously. The postoperative course was unremarkable except for a persistent one plus albuminuria. Four months later the patient had no neurologic findings except that an electroencephalogram showed a pathologic record.

COMMENT.—Factors to be considered as possibly contributing to the development of convulsions in this patient are: Hypertension; unreplaced fluid and blood loss during a major operation; and poor position on the operating table resulting from elevation of the "gallbladder bench."

Case 12.—B. S., male, age 28, was admitted to the hospital, in December, 1941, with obstructive jaundice resulting from a stricture of the common bile duct. A biliary fistula was surgically established, but soon after a celiotomy was necessary for intra-abdominal bleeding. In February, 1942, a jejunostomy was performed to facilitate feeding the patient. The final operation was performed in April, 1942. Although he had lost weight steadily, the blood picture was relatively normal, total serum protein was 6.4%, and the prothrombin level was 94%. Jaundice had disappeared. Preoperative medication of morphine 0.010 grams and atropine 0.0004 grams was given. Anesthesia was induced with nitrous oxide and maintained by ether vapor (closed mask). The "gallbladder bench" was elevated. An anastomosis of the biliary fistula to the duodenum was carried out. Eighty minutes after induction of the anesthesia convulsions appeared in the face and neck, then spread to the entire body. For a half hour before, respirations had been irregular and faster and the pulse more rapid. The anesthesia was promptly discontinued. Ten cubic centimeters of calcium gluconate (10%) was given intravenously and a blood transfusion started. After 15 minutes the convulsions stopped and five minutes later ether anesthesia, by open mask, was resumed but convulsions returned, lasting for five minutes. Anesthesia was discontinued for the next 80 minutes while the operation proceeded. During this period sodium phenobarbital 0.13 grams was given intramuscularly. Cyclopropane was given for the last 40 minutes of the operation when the patient became restless; no further convulsions occurred. Recovery of consciousness required four hours, and for the next 18 hours the patient was restless, confused, and incontinent. After the first postoperative day there were no untoward developments. Electro-encephalography 12 months later showed a normal record.

COMMENT.—This patient was a relatively poor surgical risk though an effort had been made to improve his state prior to operation. This is the only case of the series in which operation was continued for any length of time or anesthesia of any degree resumed after the convulsions. It is noteworthy that on the first attempt to resume anesthesia, convulsions promptly returned. Probably the blood transfusion, phenobarbital and long period without anesthesia (80 minutes) served to protect the patient when anesthesia was finally resumed. The rather desperate circumstances in this

case perhaps justified continuing the operation after the convulsions had occurred, but in most cases such a policy can hardly be justified. Thus, the factors to be considered as possibly contributing to the development of convulsions in this case are: Three recent operations; biliary fistula; nutritional deficiency; unreplaced fluid and blood loss during a major operation; and poor position on the operating table resulting from elevation of the "gall-bladder bench."

ANALYSIS AND EVALUATION OF THE OBSERVATIONS IN TWELVE PATIENTS

Age and Sex.—The ages of the patients varied from two to 44 years. Three were children under seven years, and the rest were 27 years, or over. One-third were males. Reviews on the subject[2, 3, 27] indicate that the incidence is higher in females,[28] and that while children and young adults both are affected, the incidence is predominantly in children.[29] With the latter our figures are not in accord, yet the ratio of children and adults coming to operation during the period of our study is representative of a cross-section of the populace. The fact remains, however, that people past the age of 50, whose basal metabolic requirements are less than those of younger people, are nearly wholly immune to convulsions during anesthesia, and it may be inferred that vascular changes, general or cerebral, occurring after middle life do not predispose to this form of operative complication.

Seasonal Variation.—One case occurred in March, two in April, two in June, three in August, two in September, and two in October. Some authors have emphasized that the convulsions have occurred during the hot summer months more frequently than at other times of the year. All of our patients were operated upon in air-conditioned rooms where constant temperature and humidity were maintained. It is suggested, therefore, that the season itself has little to do with the incidence of the convulsions, though the temperature of the operating room may be a different matter. Anesthetized persons tend to become poikilothermic and may easily become overheated in a poorly conditioned room.

Previous Convulsions.—Two of the adults had had convulsions in early childhood, and one was given to syncopal attacks under conditions of fatigue. Although some authors[9] have suspected that a predisposition to convulsions might be important as a factor in their occurrence during anesthesia, on the whole, the evidence has been unimpressive. It has often been observed that epileptics are likely to develop their convulsions during the inductions of general anesthesia or under light anesthesia,[30] but this is not to be confused with the subject under discussion. It appears paradoxical that general anesthesia, which is sometimes resorted to in the control of status epilepticus, should be responsible for convulsions in the nonepileptic.

Primary Disease and Operation.—The diagnosis in three patients was appendicitis with peritonitis; appendicectomy and drainage were performed in each. In two patients the diagnosis was chronic cholecystitis, and in one

acute cholecystitis; cholecystectomy was performed in each. In two patients there was disease of the common bile duct requiring tedious exploratory operation, with choledochostomy in one and repair of a stricture in the other. Two patients required pelvic operations, one for tubal pregnancy, the other for an ovarian cyst, and each had had preceding uterine curettage. One patient was explored abdominally for an hypernephroma with extensive metastasis to the liver. One patient, an infant of two years, underwent a long operation and difficult anesthesia for repair of a cleft palate.

Preoperative Condition of the Patient.—With regard to the condition of the patients prior to operation, hyperpyrexia which exacts an increased demand for oxygen upon all tissues of the body is of the greatest importance.[31] Payne[27] found that up to 1936, in 90 per cent of the reported cases the patients developed convulsions while being operated upon for "pyrexic disease." In our series, four of the 12 patients were acutely ill with high fever when they came to operation and, in addition, one child had not made a complete recovery from a respiratory infection. Toxicity and septicemia go hand in hand with high fever and it is probably of little use to try to separate their effects as far as the production of convulsions is concerned. However, Rosenow and Tovell[32] attributed the convulsions to a neurotoxin produced by a streptococcus which is present in amounts insufficient to cause convulsions except in the presence of general anesthesia. Dehydration and acid-base imbalance, other states which so frequently accompany febrile diseases, may contribute to the initiation of convulsions by inhibiting the cells of the brain in their ability to utilize oxygen, [33-35] Significance may be attached to the fact that many of the factors which have been thought to account for convulsions during anesthesia cause an increase in the H-ion concentration of blood and tissues.[21]

Deficiency in the nutritional state was present in at least three of our patients, two having recently gone through pregnancy, and one having lost considerable weight from the presence of a complete biliary fistula. Two patients had secondary anemia which increased the danger of anoxia during the anesthesia. In the first two patients, one of whom had peritonitis, an imbalance in calcium metabolism is to be considered as of possible importance. The effect of a low serum calcium in the production of convulsions is well known and several investigators have reported a depression in the serum calcium not only during anesthesia[36, 37] but also in acute abdominal infections.[38] Alkalosis which may result from preoperative vomiting or by overventilation during the anesthesia is also capable of disturbing the calcium balance of the blood.[39]

Position on the Operating Table.—With regard to the hazards imposed by the operative procedure itself we feel that too little attention has been paid this possibility. It can be postulated that heavy retraction of abdominal wound edges, trauma,[40] excessive exposure of viscera to cooling, loss of blood, and other circumstances that are ordinarily associated with shock and "stagnant anoxia," may be said to be conducive, as well, to the develop-

ment of convulsions. But we refer more particularly to the position of the patient on the operating table. In five of the patients the back was acutely angled by the elevation of a "gallbladder bench." Two others were placed in high Trendelenburg position to improve the exposure in the operative field. These positions mechanically impede respiratory exchange and retard circulation.[22] In one patient convulsions ceased dramatically with the lowering of a "high gallbladder bench" which had been overlooked during the distressing period when several other agents were being tried unsuccessfully in the control of the convulsions.

Preoperative Medication.—The medication used in all patients of this series was limited to a standard dose of atropine with the addition, in adults, of 10 mg. of morphine sulfate administered hypodermically 30 to 40 minutes before induction of the anesthesia. Barbiturates were not given to any of the patients preoperatively. Atropine has been implicated particularly by British anesthetists,[41, 42] and others have emphasized the danger of anoxia, particularly of the histotoxic type, with the use of moderate to large doses of morphine and barbiturate derivatives.[43] While the possible rôle of these factors is undoubtedly too little recognized they are not considered to have played any part in the production of convulsions in the patients of this series.

Anesthetic Agents.—The types of anesthesia employed in the cases reported were: "Open mask" ether in three (namely in the three children), "closed mask" ether vapor with nitrous oxide and oxygen in six cases, ethylene (with a small amount of ether vapor) in two, and cyclopropane (with a small amount of ether vapor) in one. The percentage of nitrous oxide used with ether vapor anesthesias and of ether vapor with the ethylene and cyclopropane anesthesias was relatively so little that for the sake of brevity it may be said that the anesthetic agents in this series were ether by closed and open mask, ethylene and cyclopropane. Thus, there is support for the belief that the cause of the convulsions cannot be laid to one anesthetic agent[1, 2, 10–18] or, in the case of ether, to the method by which it is administered. It may well be, as Courville[23] has suggested, that there is a certain "selectivity" by which different anesthetic agents produce their anoxic effects but the fact remains that any of the agents are capable of producing anoxia. It is to be emphasized that each patient was under deep anesthesia; perhaps several were too deep, but all were thought to be in no danger up to or near the time convulsions appeared.

Idiosyncrasy.—The possibility that some patients have an idiosyncrasy to the anesthetic agent is difficult to evaluate but some[44–46] have thought that such a state might exist, particularly with ether. Sears[47] and Kemp[48] reported instances of patients having convulsions during two different operations in which ether was used. In our series one patient had an uneventful 45-minute anesthetic two days prior to the operation during which she developed convulsions, and ether vapor, by the closed method, was used both times. Another patient had a longer and more difficult operation without convul-

sions six months after the one in which convulsions occurred, and again ether vapor, by the closed method, was used both times. These experiences, and others,[49] tend to refute arguments in favor of individual idiosyncrasy or allergy to ether.

Impurities in Ether.—With the earlier cases we were concerned, as others have been[46, 50–53] with the possibility of impurities in the ether, particularly since the ether was taken from drums. An analysis was made of the ether used in three of the cases.* The analysis in each showed: acetic acid eight parts per million; aldehyde and peroxide less than one-half per million. Tests made of control specimens of ether taken from freshly opened small cans and drums of ether showed the same values and these are far below the U. S. P. levels for impurities. No other patients given ether taken from the same drums developed convulsions. A study of 700 cases was made at the New York Hospital[54] in which it was concluded from anesthetic tests that ether does not deteriorate rapidly when open and there is no difference between the effects of fresh ether used from small cans labeled "for anesthesia" and U. S. P. ether taken from drums.

It is not our intent to imply that anesthesia plays no part in the production of convulsions but rather to emphasize that certain specific anesthetic agents cannot, to the exclusion of others, be pointed to as the offenders.

Time of the Convulsion.—It appears significant that the time found to elapse between the induction of anesthesia and the appearance of convulsions was between 40 and 90 minutes, with an average of 70 minutes. This suggests that whatever elements combine to cause the convulsions, time is required for their effects to appear. The majority of the cases heretofore reported have been of patients with acute appendicitis and the convulsions have appeared at about the time of closure of the peritoneum. However, it is believed that this time relationship is a coincidence and not otherwise important unless it be assumed that sometimes the deepening of the anesthesia for closure of the peritoneum plays some rôle.

Warning Signs.—In none of the patients was there any cyanosis observed prior to the onset of convulsions and in four there were no untoward signs of any kind. In two there were respiratory changes only, such as "labored," "jerky," "increased" breathing. In four there was, in addition to respiratory changes, a significant increase in cardiac rate. In only two were there impressive changes in respiration, increase in cardiac rate and rise in blood pressure. The changes noted usually occurred gradually over a period of 20 to 30 minutes but in other instances they developed within 5 to 10 minutes prior to the convulsions. The appearance of cyanosis is too often relied upon as the early sign of insufficient oxygenation during anesthesia though it has been amply stressed in anesthesiology that cyanosis is neither criterion nor index of degree of anoxia. Lunsgaard and Van Slyke[55] have

* The analyses were made by Dr. Harry Gold of the Department of Pharmacology, Cornell University Medical College.

shown that cyanosis depends on the presence of a definite quantity of reduced hemoglobin in the blood and not upon relative proportions of reduced and oxygenated blood. Subclinical anoxia can exist without cyanosis and yet be of a degree that would be serious, if prolonged. More significant of developing anoxia is an increase in rate and amplitude of respiration, combined with gradual rise in blood pressure and cardiac rate with variation in the volume of the pulse beats.[24]

Temperature Increase.—Only one of the patients gave evidence prior to the onset of convulsions of developing an increase in body temperature and in this patient nearly an hour passed between the appearance of hyperthermia and convulsions. Eight other patients had fever of 40° C., or more, some time after convulsions developed but three had little or no elevation of temperature at any time. There can be little doubt that under the conditions of increased body temperature, whether it be due to fever, overdose of atropine or external heat, patients, and especially children, are more prone to develop convulsions.[21] It is also true that convulsions of themselves cause an increase in body temperature. Some authors have held that an increase in body temperature was almost a prerequisite to the development of convulsions during anesthesia[56–58] but in our series one-half of the patients gave no evidence of increased body temperature, at least until some time after the seizure.

Duration of Convulsions.—The convulsions in all cases followed the same pattern, beginning in the face and spreading to the entire body. Single continuous convulsions lasted for periods varying from a few minutes to 90 minutes. In some patients there were recurring attacks over a period of hours, the longest period being 40 hours. In general, it may be said that the longer the single attack lasts or the longer the period of recurring attacks, the less chance that the patient will recover.

Mortality and Autopsy Findings.—Death occurred in three patients, making a mortality rate for the series of 25 per cent. Autopsy was performed on one of these three (Case 9), and as far as the routine examination of the brain is concerned, no notable changes were found except a moderate degree of congestion as evidenced by dilatation of the small pial vessels. More impressive changes were disclosed in other organs, such as acute pulmonary congestion and atelectasis of one entire lung, congestion in the kidneys, and petechial hemorrhages in the myocardium, pericardium and pleura. The pathology found is compatible with that described by Courville[1] in the patients dying from anoxia with nitrous oxide anesthesia. Unrecognized atelectasis must always be considered as the possible source of trouble when convulsions develop during the operation.[59]

While it would support our belief that anoxia was responsible for the convulsions and death in this patient if more impressive pathology could be demonstrated in the brain, it is likely that death occurred before detectable changes had an opportunity to develop. Courville[1] states that "changes in the nerve cells or in interstitial tissues are not characteristic until 36 to 40

hours have elapsed, time sufficient for physicochemical changes incident to anoxemia to become evident histologically."

Morbidity.—All the patients who did not die showed either delayed recovery from anesthesia or late sequelae or, both. Delayed recovery was characterized principally by slow return to consciousness, restlessness, irrationality, delirium, confusion, uncooperativeness, incontinence. One patient has what appears to be permanent changes in temperament and personality while another has a residual hemiparesis. In the case of hemiparesis, while it is likely that a cerebral vascular accident occurred, Behrend and Riggs[20] have emphasized that individual variations in the cerebral vasculature are often the cause of clinical symptoms being referred to one side, even in the presence of diffuse cerebral damage. A lumbar puncture is of little diagnostic value since convulsions alone are often the cause of transitory increased intracranial pressure and red blood cells in the cerebrospinal fluid.

Electro-encephalographic Changes.—It has been especially illuminating to find that in four of the seven patients subjected to electro-encephalography at varying periods after their operations, there were pathologic changes recorded. It would be useful to know whether changes which may be found early after the convulsive episode would persist but our data does not supply this information. Also, it would be necessary always to take into consideration the possibility that patients may have had abnormal brain waves prior to the time of the operation.

Other Effects of Anoxia.—The clinical evidence for damage to other organs of the body as a result of the anoxia, presumed to have caused the convulsions, is to be found in the high incidence of postoperative pulmonary complications (in seven of the ten patients who lived longer than a day after operation) and of albuminuria (in five of the ten).

Blood Studies.—Various blood studies made soon and late after the occurrence of convulsions in a number of the patients failed to disclose any significant changes. But no blood oxygen determinations were made and it is highly desirable in order to establish the importance of anoxia that more studies be pursued comparable to those of McClure, *et al.*[43] in which changes in the oxygen content, capacity and saturation of the arterial blood were evaluated under various conditions of anesthesia.

DISCUSSION

The stage has perhaps not yet been reached at which the evidence can be said undisputably always to point to anoxia as the state underlying the occurrence of convulsions during anesthesia, yet the bulk of the collected data points in this direction. Since the brain cells and particularly those of the cerebral cortex are more susceptible to anoxia than other tissues of the body it is easy to explain the early occurrence of convulsions.

Barcroft's[60] classification of the anoxemias, based on physiologic principles, is useful in attempting to understand the many factors that must be evaluated in clinical cases. In the *anemic type,* present in patients with lack

of, or inactivation of hemoglobin, the red blood cells do not carry a normal amount of oxygen, although oxygen tension in the blood may be normal. In the *stagnant type,* because of slowed circulation, the oxygen supplied to the tissues is reduced. In the *anoxic type,* oxygen tension in the blood is lowered so that there is actually less oxygen in solution and because of an associated lowering of carbon dioxide tension there is decrease in the rate

TABLE I

FACTORS INFLUENCING THE ANOXIC STATE AND DEVELOPMENT OF CONVULSIONS DURING ANESTHESIA

Factors Pertaining to Individual Susceptibility
- Youth
- Female sex
- Convulsive diatheses

Factors Pertaining to the Anesthetic Agents
- Probably moderate anoxia upon which the production of the anesthetic state depends
- Too deep anesthesia
- Combination of anesthetic agents
- Impurities in the anesthetic agent
- Impure oxygen
- Overoxygenation
- Too much or too little carbon dioxide
- Imperfections in the anesthetic machine

Factors That Increase the Oxygen Requirement of the Body Tissues
- Fever
- Heavy blanketing of patient
- Overheated operating room
- Hot weather

Factors That Disturb Circulation of Blood
- Cardiac disease
- Vascular hyper- or hypotension
- Cerebral vascular accident
- Reduced blood volume
- Hemorrhage

Factors That Disturb Respiratory Exchange
- Obstruction to air passages
- Faulty aeration of lungs
- Deficient alveolar absorption
- Poor position of patient on operating table
- Obesity

Factors Affecting the Oxygen-Carrying Properties of the Blood
- Anemia
- Poisoning (as carbon monoxide)
- Sulfonamide therapy

Factors Which Possibly Affect the Tissue Cells' Ability Specifically to Utilize Oxygen
- Acid-base imbalance
- Dehydration
- Hypoglycemia
- Calcium imbalance
- Nutritional deficiencies
- Sedatives, opiates, atropine
- Neurotoxin

of dissociation of oxyhemoglobin, all resulting in less readily available oxygen for the tissues. This type of anoxia may result from reduced oxygen in inspired air, obstruction in the air passages, faulty aeration of the lungs (as in atelectasis of the lungs) deficient absorption of oxygen from the lungs (as in pneumonia) or inability of the blood to carry a sufficient quantity of oxygen (as in the presence of methemoglobin). To these, Peters and Van Slyke[61] have added the *histotoxic type* in which the tissue cells of the body, due to toxins or drugs,[43] are less able to utilize the available oxygen.

It seems useful, then, to enumerate the various possible clinical factors that may contribute to the anoxic state and to the development of convulsions during operations in which general anesthesia is employed (Table I).

The inadequacy of this or any classification is well appreciated; it does not purport to be entirely original or complete. The placing of some of the factors under one heading and not under others is in many instances arbitrary; furthermore, some of those mentioned may be of no importance. But some order may thus be lent to the confusion existing over the numerous etiologic factors and it may more easily be seen that while one factor alone may be insufficient cause for the development of anoxia, the effects of two or more may readily be combined under the varied conditions of disease, operation and general anesthesia.

TREATMENT

Convulsions during anesthesia are relatively rare and probably much less frequent than other less dramatic effects of anoxia. A discussion such as this serves principally to draw attention to the nature of the state and the possibilities for its prevention by employing adequate preventive measures both before and during the operation.

When convulsions do occur it is advisable to (1) discontinue the anesthetic, (2) terminate the operation as quickly as possible; (3) administer oxygen; (4) correct any unfavorable position on the operating table; (5) keep the airway open (bronchoscopic aspiration may be required in case of atelectasis); (6) give some form of soluble barbiturate intravenously to control the convulsions, such as sodium amytal, sodium phenobarbital, or pentothal sodium; (7) replace blood or fluid loss; and (8) allay hyperthermia by sponging the body or irrigating the rectum with cold water. An oxygen tent provides the dual service of cooling and supplying adequate oxygen. There may be advantage in administering hypertonic glucose solution intravenously, particularly to combat unrecognized hypoglycemia and intravenous calcium gluconate or intramuscular parathormone to correct calcium imbalance.

SUMMARY AND CONCLUSIONS

An analysis of 12 cases in which convulsions occurred during general anesthesia shows:

1. Convulsions occur in about one in 6,000 patients subjected to general anesthesia.

2. The mortality rate is 25 per cent—too high to be the result of convulsions alone.

3. The term "ether convulsions" is misleading since the convulsions may occur during other types of general anesthesia.

4. Most of the alleged causes of the convulsions are not of a nature to be alone or directly responsible. But most of them bear some relationship

to the delivery, transportation and utilization of oxygen for tissue respiration, thus suggesting anoxia as the chief factor in precipitating the convulsions.

5. Since the cells of the brain are more sensitive to anoxia, convulsions often appear before other signs but when convulsions do appear an advanced state of anoxia may already exist.

6. The incidence of convulsions during anesthesia may be lowered by attention to the preparation of the patient for operation; to the proper administration of the anesthetic and to the contributing effects of the operation itself.

7. When convulsions occur all measures should be directed toward correction of the causative factors and alleviation of the state of anoxia. Some form of barbiturate should be given intravenously to control the convulsions.

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ACUTE POSTOPERATIVE NECROSIS OF THE LIVER*

AN EXPERIMENTAL STUDY

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REPORTS by the writer,[1, 2] in 1935 and 1936, dealt with acute postoperative necrosis of the liver in dogs following ligation of the hepatic artery. At that time two general conclusions were drawn: First, that so-called "high temperature liver death syndrome" is a clinical entity characterized by rapid progressive development of high temperature, falling blood pressure, circulatory collapse, coma and death, with a temperature as high as 109° F. (human) within 36 to 48 hours after operation; and, second, that the essential lesion in the liver is diffuse central necrosis of the liver lobules. This syndrome was first described by Heyd,[3] in 1924, and has been known since that time as "acute liver death," "high temperature liver death," "acute liver insufficiency," and the "hepatorenal syndrome." Autopsies have shown diffuse focal necrosis in the liver but no other lesions competent to produce the severe symptoms and the rapid death. The liver shows passive congestion, softening, and diffuse disorganization of the liver cords, with widespread areas of focal necrosis. Boyce,[4] and Boyce and McFetridge[5] concluded that in most instances when the clinical course is typical, the postmortem findings are typical, *i.e.*, necrotic changes in the liver with or without similar changes in the convoluted tubules of the kidneys, depending upon how long the patient lived after operation.

Experimental ligation of the hepatic artery produced typical lesions in, and rapid death of healthy dogs[1, 2] when adequate collateral circulations did not exist. However, from this fact it can not be argued that this is the mechanism which produces necrosis of the liver in human beings. It does seem reasonable, nevertheless, to believe that the lesion is related in some way to conditions affecting the hepatic artery. Necrosis of the liver sometimes follows operations on the stomach, pancreas and other abdominal viscera and is frequently present in death of thyroid crisis.[6] It may be that there is some common factor which links together necrosis of the liver, biliary tract surgery, operations upon the stomach, pancreas and other abdominal viscera and thyroid crises.

The vasoconstrictor nerves of the hepatic artery are derived from branches of the celiac plexus, and in their course to the liver are closely related to the extrahepatic blood vessels and the bile ducts. Therefore, these nerves are directly in the field of operations upon the bile ducts

* Presented before the joint meeting of the Philadelphia Academy of Surgery, and the New York Surgical Society in New York, February 10, 1943.

and the gallbladder, and during such operations are subjected to trauma. In his exhaustive work on the vasomotors of the liver, Opitz[7] demonstrated (1911) almost complete interruption of blood flow through the hepatic artery following faradic stimulation of branches of the celiac plexus.

Experiments were undertaken to determine the effect upon the liver of mechanical stimulation of the branches of the celiac plexus. In healthy dogs these nerves were mauled, clamped, pinched and roughly sponged. The immediate gross effect on the liver was the same as followed ligation of the hepatic artery. The surface of the liver became irregular in color, blackish in spots, and in other areas a mosaic discoloration appeared. In these areas it appeared as though the liver lobules were outlined by small black lines. These livers were of normal healthy dogs. No syndrome developed and the postoperative courses were smooth.

It is an accepted fact that disease of the gallbladder and the bile ducts is accompanied by hepatitis, and that each successive exacerbation of the biliary tract disease adds to the lesions in the liver. This must result in progressive impairment of liver function, but the factors of safety are so great that a liver may give no clinical or laboratory evidence of severe damage. Under the normal stress of living, these livers may function in an adequate manner, but under the abnormal strain of an operation and anesthetic, the slim reserve may be exhausted.

In order to conduct experiments in a satisfactory study of the effects of operations upon the gallbladder and bile ducts, comparable to the results in human beings, the experimental animals must have impaired liver function or liver damage. This impairment must be chronic, of slow development, and of such a nature as to allow the animal to live in an apparently normal manner.

Rousselot and Thompson[8] (1939), in a study on "Experimental Production of Congestive Splenomegaly," induced cirrhosis of the liver in normal dogs by injecting a saline suspension of silicon dioxide into the splenic vein. Cirrhosis of the liver developed only after enough silica had been given, and enough time had elapsed to allow development of the lesion in the liver. In this study, the technic used by Rousselot and Thompson was used.

Twelve normal, healthy, adult male cats were used in the experiments. At celiotomy, 25 to 50 cc. of a sterile saline suspension of silicon dioxide* (one per cent) was injected slowly into the splenic vein. At intervals of six weeks a second and a third injection of the silicon dioxide suspension was made in the splenic vein of each cat. At the second operation, well developed gross silicosis of the hepatic regional lymph nodes was evident in each animal, and at the third operation there was beginning gross evidence of cirrhosis of the liver. Nine cats died at various periods during

* Silicon dioxide suspension, one gram in 100 cc. normal saline. The individual silicious particles are 1–3 micra in diameter.

The silica was prepared by Dr. Leroy U. Gardner, Director of the Saranac Laboratories, Saranac, N. Y.

FIG. 1.

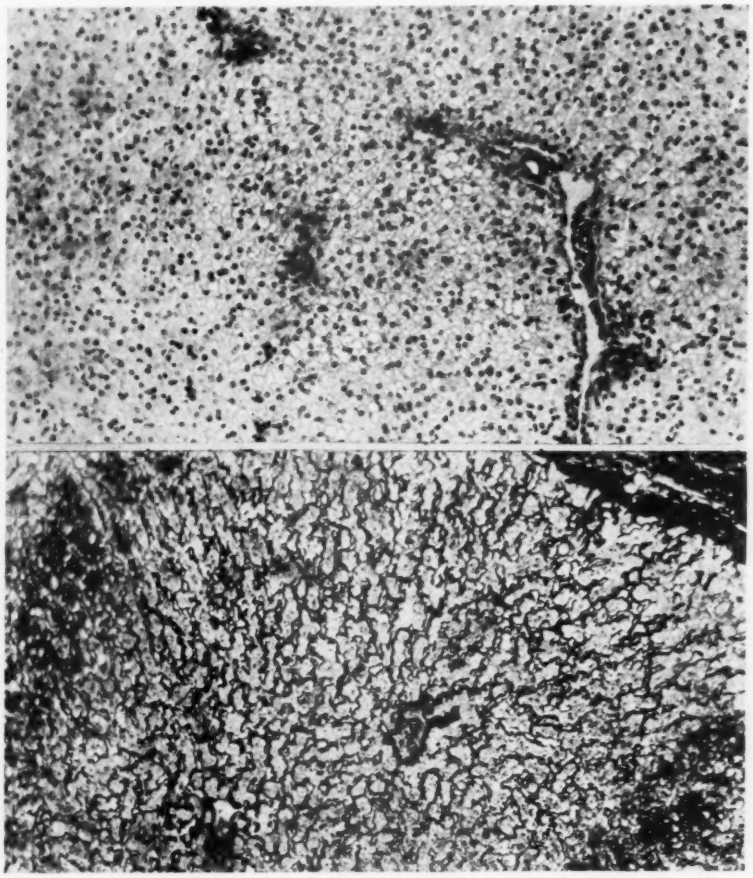

FIG. 2.

FIG. 1.—Normal liver, cat: Trichlorsilver stain shows no intrahepatic connective tissue. (×225)

FIG. 2.—Experimental cirrhosis of the liver, cat: Connective tissue (black), demonstrated by trichlorsilver stain, is widespread, and encloses the cords of liver cells. (×225)

the time necessary to induce cirrhosis of the liver, and sections of their livers showed cirrhosis in direct proportion to the degree of silicosis of the regional lymph nodes (Figs. 1 and 2).

Three cats which received three injections of saline suspension of silicon dioxide, lived through the summer months, and appeared to be in good condition for the concluding experiment. At the operation, each cat showed gross cirrhosis of the liver with ascites. In each case a cholesystectomy, from cystic duct to fundus, was performed, and this was immediately followed by intermittent stimulation of the branches of the celiac plexus with faradic current from an induction coil, for two minutes. Each cat died promptly, in less than 18 hours after operation. Autopsies

showed congestion of the liver, and areas of softening. There was no hemorrhage, thrombosis or other cause of death. A clinical thermometer sewed in the abdominal cavity at the conclusion of the operation did not show any rise of temperature. Microscopic sections of these livers (Fig. 3) show congestion and diffuse focal necrosis.

Three normal, healthy adult male cats were used as controls. The same procedure (cholecystectomy and faradic stimulation of branches of the celiac plexus for two minutes) was used. All of these animals survived for an indefinite period following the operation and nerve stimulation. A second operation was performed on one of the controls. At the first operation a small gauze sponge was left in the subhepatic region. At the

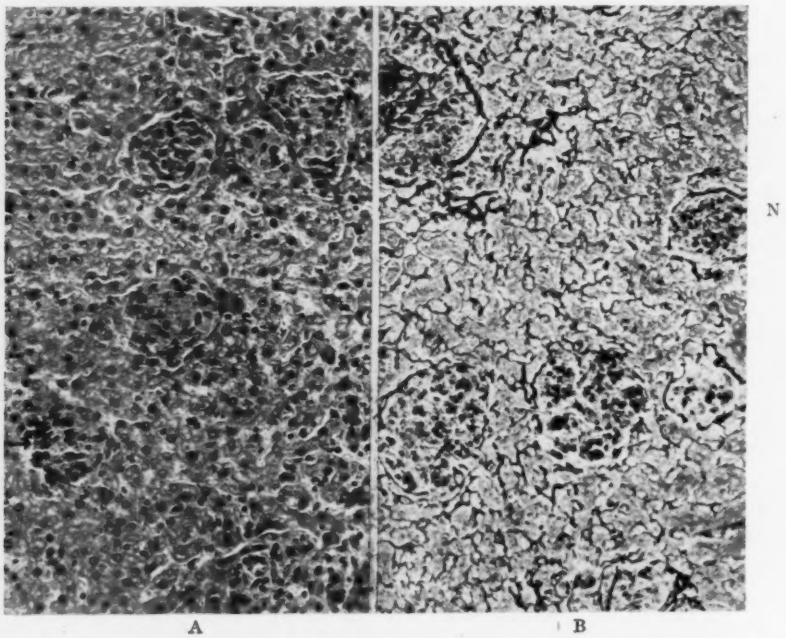

FIG. 3.—Liver of cat in which experimental cirrhosis was produced: Death followed farradic stimulation of branches of the celiac plexus. (×225)
(A) Hematoxylin and eosin stain. Circular areas of liver necrosis (N).
(B) Trichlorsilver stain of the same liver. Note circular areas of nectotic cells (N), outlined by connective tissue.

second operation the liver, stomach, bile ducts and intestines were involved in many dense adhesions. Separation of these adhesions to expose the bile ducts and the celiac plexus produced severe trauma. Faradic stimulation of the nerves for two minutes produced no effect, and the animal made an uneventful recovery.

The microscopic pictures of the livers of (1) human beings dying a "liver death;" (2) dogs following ligation of the hepatic artery; and (3) cats with cirrhosis of the liver, which have died following cholecystectomy and intermittent faradic stimulation of the celiac plexus, are the same. They

show diffuse focal necrosis of the liver. It seems reasonable, therefore, to conclude that fundamental cause of the so-called "liver death" syndrome is a badly damaged liver. Stimulation of branches of the celiac plexus, during operations upon the gallbladder and bile ducts, produces spasm of the hepatic artery. This spasm deprives the liver of its arterial blood supply (Opitz[7]) and an irreversible reaction is initiated, which results in diffuse focal necrosis of the liver. It also seems reasonable to conclude that the essential pathologic lesion in the liver of human beings, dogs, and cats is the same—diffuse focal necrosis.

Local injections of novocain in the gastrohepatic omentum anterior to the foramen of Winslow or novocain block of the celiac plexus should prevent impulses traveling along these nerves to the liver. Although, in this study, no experimental nerve or plexus blocks have been performed, I believe that such measures should be used when one encounters a firm, irregular liver or gross evidence of cirrhosis, if biliary tract surgery is contemplated.

Grateful acknowledgment is made to Dr. Allen O. Whipple for the opportunity to undertake this work in his department; to Dr. Arthur Purdy Stout, for suggestions and examination of specimens; to Major Louis M. Rousselot, M.R.C., U. S. Army, for assistance and suggestions; and to Miss Daisy Mapes for assistance and care of the animals.

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BRIEF COMMUNICATIONS

MASSIVE FIBROMA OF THE SCALP

CASE REPORT

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THIS CASE is presented because of the size and peculiar appearance of the tumor, and also because of the surgical problem involved.

Case Report.—G. D., white, male, age 23, entered the Saskatoon City Hospital complaining of a growth covering a large portion of the right side of his head. The mass had been present since birth and had enlarged as he had grown. For the past several years it had remained practically stationary. He had been advised against operation, because of the danger of hemorrhage. He had been rejected for service in the army. We felt it was of great importance to the future of this young man if this mass could be removed successfully. It is self-evident that such a glaring deformity must give anyone an inferiority complex.

The general examination and history were irrelevant. Examination of the mass revealed a partly lobulated growth, 16 cm. in length, 12 cm. in width, while the

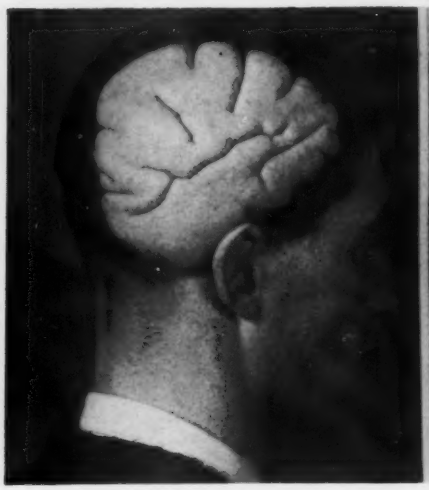

FIG. 1.—Lateral view of fibroma prior to operation.

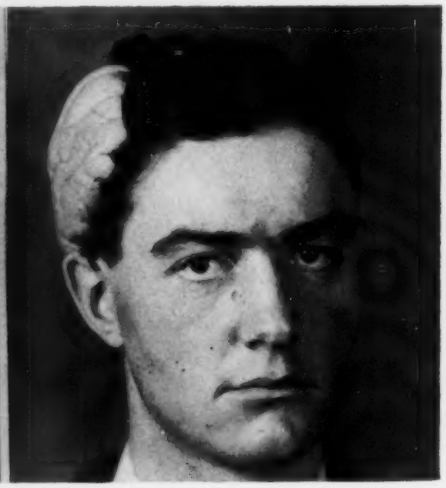

FIG. 2.—Anterior view of fibroma prior to operation.

greatest thickness was almost 5 cm. The surface was smooth and hairless, but was indented quite deeply by characteristic sulci which, with the pale pinkish color, gave it the appearance of exposed cortex. The mass was very hard, though slightly movable, but was attached to the scalp completely to its actual periphery. The growth of normal scalp hair ended abruptly at the exact border of the tumor (Figs. 1 and 2). Roentgenograms demonstrated no involvement of the skull.

Surgical Procedures.—January 9, 1942: Biopsy was performed, and the sections were reported upon by Dr. W. S. Lindsay, pathologist, University of Saskatchewan, as follows: *Pathologic Examination.—Microscopic:* Section shows a thin but uniform and typical covering of stratified squamous epithelium. Beneath this is an interlacing mass

of dense strands of collagen with few fibrocytes. In many of these strands there is a vessel or slit lined by endothelium which is thickened and shows some activity, and masses of endothelial cells are found embedded in the fibrous strands (Fig. 3). *Pathologic Diagnosis:* Lymphangiofibroma — no evidence of malignancy. Keloid.

January 12, 1942: The scalp was infiltrated with 1% novocain solution. The removal of the tumor was commenced by electro-section at its posterior border. The very numerous vessels were coagulated at once. However, it was soon evident that the heat penetrated to the skull, though the usual precautions were used. The entire central mass of the tumor was, therefore, removed leaving a mat one centimeter in thickness and the rim of the tumor almost intact (Fig. 4). The raw surface was dressed with vaseline gauze.

January 17, 1942: Again using local anesthesia, the entire floor of the tumor was removed, together with a considerable of the edge of the tumor. The border of the tumor was now raised and loosened. Because of its density, silk sutures could be inserted and drawn very tightly. This allowed us to displace the periphery of the tumor, so as to reduce the uncovered area (Fig. 5).

February 5, 1942: Under general anesthesia, the previous tension sutures were removed and the remaining edge of the tumor excised. Hemorrhage was of considerable moment, many of the vessels being so large that ligation was necessary, as they could not be successfully occluded by coagulation.

The scalp was now loosened over the vertex, forward over the frontal region, and backward, freeing most of the occipital area. The neck tissues were undercut

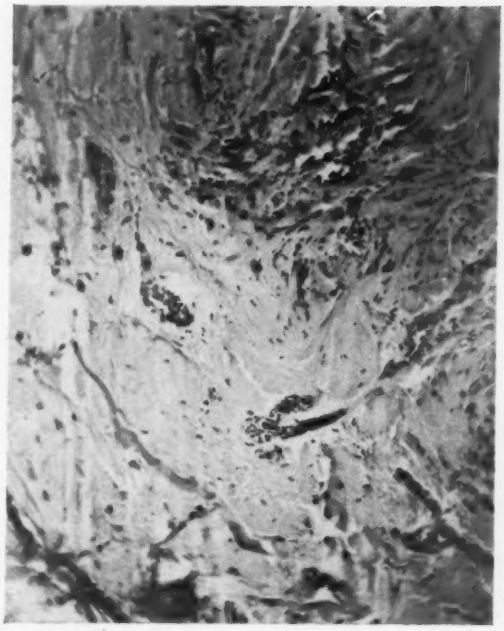

FIG. 3.—Pathologic section of fibroma showing fibrous tissue and vessels lined with endothelial tissue.

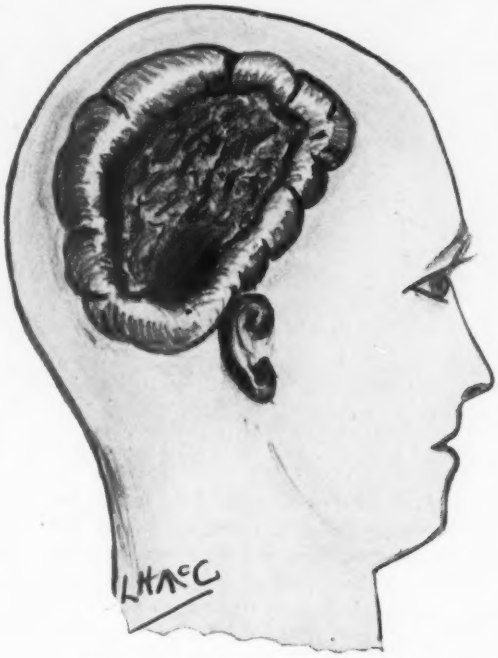

FIG. 4.—Appearance after first operation.

behind the right mastoid. A linear incision was made in the mid-occipital region as well as a prolongation of each edge of the excised area downward and backwards behind the right mastoid.

The scalp was now stretched by strong traction and sutured (Fig. 6). Happily, this patient had a fairly loose, pliable scalp. The full use of the above measure reduced the uncovered area to a triangular space 5 x 10 cm.

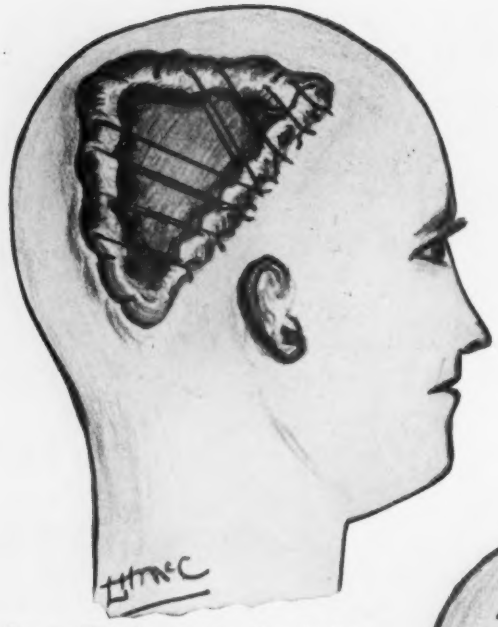

FIG. 5.—Following 2nd operation, showing tension sutures.

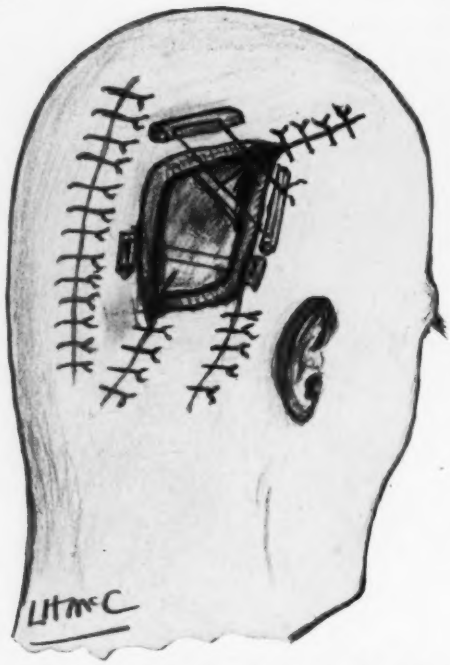

FIG. 6.—Following 3rd operation, showing incisions necessary for plastic attempt.

Postoperative Course.—The tension sutures were removed after two weeks, and the area grafted with foreskins removed at circumcisions. The mucous membrane being first removed, each specimen was sectioned conveniently into six pieces and applied and covered with a dressing of Ringer's solution. About two-thirds of the grafts were successful. The area was completely covered by March 30, 1942 (Fig. 7). After his hair had regrown, he returned to show us the result. He is very grateful because of his changed appearance (Fig. 8).

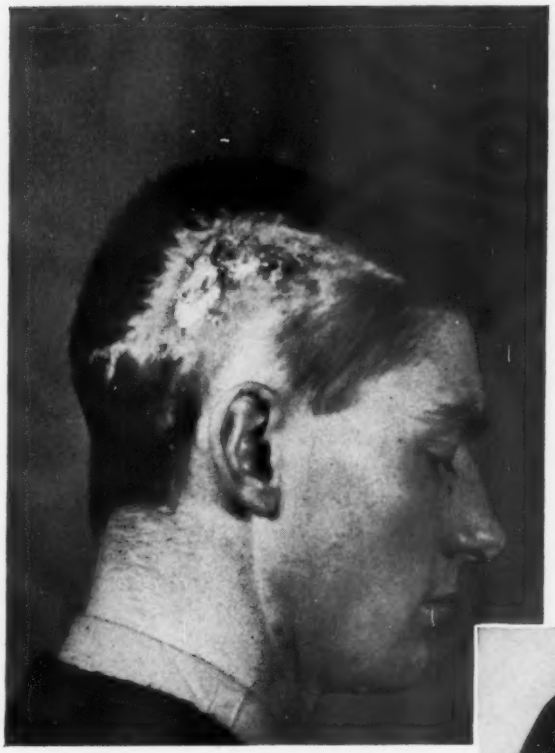

FIG. 7.—Appearance on discharge.

FIG. 8.—Nine months following operation.

SUMMARY

A large fibroma of the scalp, of unusual appearance, is reported, and the stages of its removal described. Photographs and drawings are presented illustrating the work done. Careful planning of each procedure is of the greatest importance.

A METHOD OF FIXATION FOR FRACTURES OF THE STERNUM*

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CANADA

FRACTURES OF THE STERNUM are comparatively rare. Those with displacement frequently cause serious disability. The most common site of injury is probably the junction of the manubrium with the body of the sternum.

The stooping posture of the patient is characteristic. Complaints of upper substernal pain associated with dyspnea are suggestive of such an injury. There may be deformity, but this is easily obscured by swelling,

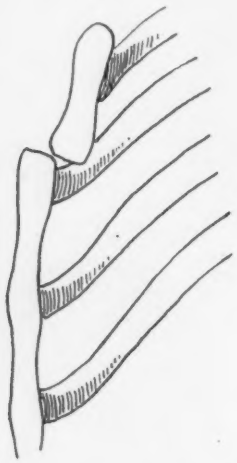

FIG. 1.—Sketch from roentgenogram (retouched) showing the fracture-dislocation of the sternum, with backward displacement of the manubrium.

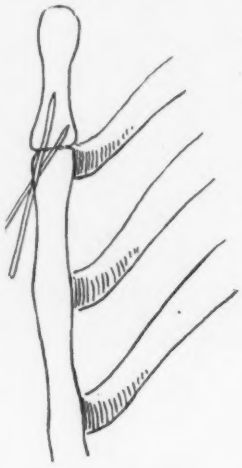

FIG. 3.—Sketch from postoperative roentgenogram showing complete reduction, with the wires in place.

while the natural variations in the prominence of that portion of the sternum render this sign of somewhat lesser importance. There is localized tenderness at the point of injury, but the tenderness is sometimes more widespread due to concomitant injuries to the sternochondral articulations.

Satisfactory roentgenograms are difficult to obtain, and the patient should not be subjected to too much movement for roentgenologic investigation until he has recovered from his initial shock, which is sometimes very considerable.

Rupture of the internal mammary artery has been reported as a complication.[1] Spontaneous reduction is said to sometimes occur on coughing

* Permission to publish this article has been granted by the Department of National Defense, Ottawa, Canada. Brigadier J. C. Meakins, Deputy Director-General of Medical Services.

or sneezing.[2] Some cases can be reduced by manipulation in the position of upper dorsal hyperextension, with the head and shoulders hanging over the edge of a table. Other cases require open operation and sometimes fixation to maintain reduction. Such a case is herewith reported:

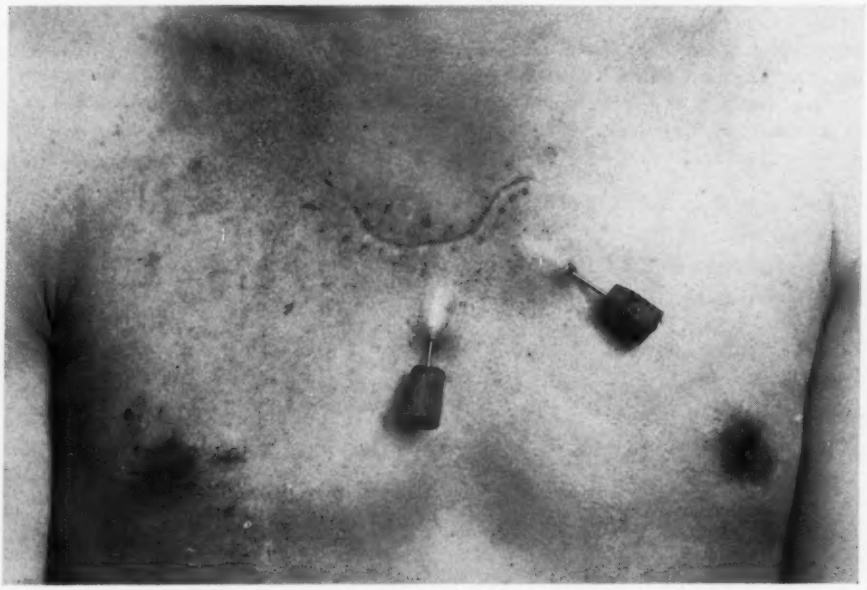

FIG. 2.—Photograph showing site of incision, and the management of the Kirschner wires.

Case Report.—Lieut. J. T. was admitted, November 18, 1942, suffering from injuries received in a motorcycle accident. There was a history of a brief loss of consciousness.

Examination showd multiple lacerations and contusion of the face, scalp, right arm and anterior chest wall. He complained of pain on compression of the upper chest. These complaints were thought to be explainable by the multiple contusions present. There was a moderate degree of shock. Roentgenograms of the skull showed no fracture.

Six days later his thoracic pain became more localized in the region of the upper portion of the anterior chest wall. The other areas of contusion were no longer complained of but he felt a constant sense of substernal distress, with dyspnea, especially on movement. A definite area of tenderness at the manubriosternal junction could not be quite sharply localized. As he could now be moved without too much discomfort, more extensive roentgenologic examination was carried out, and it was possible to demonstrate a fracture-dislocation of the sternum, with backward displacement of the manubrium (Fig. 1). Even with the knowledge so gained, the displacement could not be made out by palpation.

Attempts at reduction by hyperextension were unsuccessful, and open reduction was considered necessary. Operation was performed on November 27, 1942, nine days after injury, under local anesthesia. The fracture line was exposed by a short curved incision about one inch below the point of fracture. The depressed portion (manubrium) was elevated, but owing to a sloping fracture involving the posterior surface of the lower fragment, reduction could not be maintained and fixation was necessary. This was

accomplished by a Kirschner wire, which was inserted through a point about two inches below the incision in the skin and passed upwards through the body of the sternum to cross the fracture line and penetrate superficially into the manubrium.

A second wire was passed transversely through the sternum and into the end of the second rib on the right side. This was made necessary by a complete detachment at the second chondrosternal articulation. The wires were allowed to project about three-quarters of an inch from the skin, and corks were applied to their ends (Fig. 2). A postoperative roentgenogram showed complete reduction, with the wires in place (Fig. 3). The skin wound healed *per primam*. The wires were removed December 24, 1942, four weeks after insertion, and the patient was permitted to leave the Hospital for sick furlough four days later. The complete and permanent relief of all symptoms from the moment of reduction was quite spectacular.

To the best of my knowledge, this method of fixation has not previously been reported. While it is probable that many cases requiring open reduction need no fixation, the simplicity and effectiveness of this method, when necessary, is considered sufficient excuse for its publication.

SUMMARY

A case of fracture of the sternum with posterior displacement of the manubrium is reported.

A simple and effective method of fixation after reduction is described.

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